The Effects of Air Pollution on Mental Health and Well-being

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Declarations and Statements

DECLARATION

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed.....[redacted]..

Date...............19/12/2023...

STATEMENT 1

This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

Signed.....[redacted]..

Date...............19/12/2023...

STATEMENT 2

I hereby give consent for my thesis, if accepted, to be available for photocopying and for inter-library loan, and for the title and summary to be made available to outside organisations.

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The University's ethical procedures have been followed and, where appropriate, that ethical approval has been granted.

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Abstract

Air pollution is a significant environmental risk to human health. Historically, the impact of air pollution has focused upon the physical health effects, yet the implications on mental health have received limited attention. Despite this, recent research has highlighted emerging evidence supporting a possible aetiological link. The purpose of this study, therefore, was to investigate the potential consequences of air pollution upon various mental health and well-being issues.

In a PRISMA based systematic review multiple databases were searched from January 2012 to 2022 for peer-reviewed, English-language, human based primary research. Of the 2,224 studies identified in the literature search, 87 met the inclusion criteria. The mental health and well-being issues explored were psychosis, anxiety, suicide, mania, hospital visits, and self-reported well-being. Depression was omitted due to a recent systematic review on the condition. The key pollutants investigated as described by the World Health Organisation (2021) were particulate matter (PM_{10} and $PM_{2.5}$), sulphur oxides (SO_x), carbon monoxide (CO) and nitrogen oxides (NO_x). Data from the review revealed air pollution could have adverse effects on various mental health and well-being issues (suicide, anxiety, life satisfaction). The key finding was the positive association between PM and NO_2 on stress and psychotic disorders. However, a negative impact from air pollutants for some of the mental health outcomes was less clear because of a lack of research (*e.g.,* mania and self-harm) and contradictory findings (*e.g.,* anxiety and suicide). Overall, the most noted effect was the positive association between psychotic disorders and NO_x which was demonstrated in ten studies with only one contradictory finding.

These results were further investigated by Secure Anonymised Information Linkage (SAIL) because of the heterogeneity of the studies in the review. SAIL contains anonymised longitudinal, routinely collected, health, social, and environmental data on the Welsh population. Therefore, an indication of real-life associations was explored between psychotic disorder diagnoses and $PM_{2.5}$, PM_{10}, NO_x. A weak positive correlation was found between $PM_{2.5}$ and the percentage of schizophrenia or other psychotic disorders (OPD). Whereas a weak negative correlation and no correlation was found for PM_{10} and NO_x respectively. The descriptive statistics generated found more than double the number of people with psychotic disorders in the most deprived compared to the least deprived areas. In contrast, sex, age and rural or city residence did not show much variation between the schizophrenia or OPD cohort and the whole population.

In conclusion, the overall findings indicate that PM and NO_2 were the most hazardous pollutants to well-being *e.g.,* stress, and severe mental disorders *e.g.,* schizophrenia. Additionally, knowledge gaps were identified such as how deprivation could affect potential associations and the causal mechanism. More high-quality research is required due to limited and some contradictory findings. Overall, the evidence suggests reducing air pollution could have benefits for physical and mental health.

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Abbreviations and Ontology

Abbreviation (if applicable)	Term in full	Working Definition (if applicable)
BPRS	Brief Psychiatric Rating Scale (linked)	A tool clinicians or researchers use to measure psychiatric symptoms (Psychiatric Times, 2021).
CI	Confidence Interval	A range of estimates for an unknown parameter.
CCI	Crown-Crisp Index	Phobic anxiety scale which consists of eight self-rated questions about fearfulness and desire for avoidance of common situations or environments (Crown & Crisp, 1966).
CMHS	Community mental health service	Support or treat people with mental disorders in a domiciliary setting, instead of institutional settings.
CNS	Central nervous system	Is made up of the brain and spinal cord. The brain controls thinking, learning, moving, and feeling. The spinal cord carries messages back and forth between the brain and the nerves that run throughout the body.
DSM	Diagnostic Statistical Manual	Used by clinicians and researchers to diagnose and classify only mental disorders. Different versions dependent on the year published.
ESS	Early Signs Scale	Self-assesses the risk of relapse from schizophrenia.
GAD	Generalized Anxiety Disorder Scale- GAD-7 and GAD-2 (linked)	Diagnostic tool validated in both the primary care setting and the general population (Löwe *et al.,* 2008). The GAD-2 is an ultra-quick version of the seven-item scale that incorporates the first two questions of GAD-7, which are critical

		components of any anxiety disorder (Sapra *et al.,* 2020).
GP	General practitioner; primary care physician	Treat all common medical conditions and refer patients to hospitals and other medical services for urgent and specialist treatment. Typically, the entry point into the health care system
HADS	[Hospital Anxiety and Depression Scale](#) (linked)	A self-assessment scale developed and found to be a reliable instrument for detecting states of depression and anxiety in the setting of a hospital medical outpatient clinic.
ICD	International Classification of Diseases.	Allows the systematic recording, analysis, interpretation and comparison of mortality and morbidity data collected in different countries or areas and at different times. Different versions 9 and 10.
ICD-CM	International Classification of Diseases- clinical Modification	A system used by physicians and other healthcare providers to classify and code all diagnoses, symptoms and procedures recorded in conjunction with hospital care.
ICPC	International Classification of Primary Care	Classification method for primary care encounters.
IGRP	Information Governance Review Panel	Reviews proposals and gives approval to those that want to access SAIL data.
IQR	Interquartile range	The difference between the upper quartile (third quartile) and the lower quartile (first quartile) in an ordered data set.
-	Lag	A period of time between one event and another.
-	Longitudinal	Over time.
LUR	Land Use Regression	Statistical method, which uses geospatial data to develop prediction models in environmental and health sciences.

MASC	Multidimensional Anxiety Scale for Children	A tool for self-assessment of anxiety dimensions in children and adolescents aged 8 to 19 years.
NHS	National Health Service	Is the publicly funded healthcare system in the UK.
NO_2	Nitrogen dioxide	Air pollutant.
RR	Relative Risk	Is a ratio of probabilities of the event occurring in all exposed individuals versus the event occurring in all non-exposed individuals.
O_3	Ozone	Air pollutant.
Pathologize	-	Regard or treat as psychologically abnormal.
PHQ-9	Patient Health Questionaire (linked)	Short screening instrument used for detection of depression in various settings, including general and mental health care as well as the general population.
PM	Particulate Matter	Everything in the air that is not a gas and therefore consists of a huge variety of chemical compounds and materials, some of which can be toxic.
SAIC	State Anxiety Inventory for children	Definitive instrument for measuring anxiety in children.
SAIL	Secure Anonymised Information Linkage	Contains anonymised longitudinal, routinely collected, health, social, and environmental, data on the Welsh population
SCAS	Spence Children's Anxiety Scale	Intended for research or clinical use under the supervision and care of a trained mental health clinician.
SCID	Structured Clinical Interview for DSM-IV	Semi structured interview created to make reliable psychiatric diagnoses in adults according to DSM-IV (Kübler *et al.,* 2013). It has two parts: one for DSM-IV Axis I

		Disorders (SCID-I) and another for DSM-IV Axis II Personality Disorders (SCID-II) (Kübler *et al.,* 2013).
-	Outpatient	A patient who attends a hospital for treatment without staying there overnight.
UFP	Ultra-fine particles	Aerosols with an aerodynamic diameter of 0.1 µm (100 nm) or less (Kwon *et al.,* 2020).
UK	United Kingdom	A state made up of the countries of England, Wales, Scotland, and Northern Ireland.
WHO	World Health Organisation	Is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring, and assessing health trends.
YMRS	**Young Mania Rating Scale (linked)**	**Self-reports the severity of manic symptoms.**

1 Introduction

The introduction of this thesis will begin by providing an understanding of mental health and well-being, then air pollution and lastly the link between the environment and mental health. The complexity of defining and categorising the diverse as well as overlapping types of mental health issues will be discussed. Topics covered in this section will be the lack of research into mental health compared to physical health as well as their unknown aetiology. Air pollution will also be defined, and the numerous physiological consequences explained. Evidence linking mental health and air pollution will be discussed via the potential mechanisms and research. This thesis will emphasise the serious threat of air pollution to human health in parallel with the World Health Organisation (WHO) report in 2021. In addition to the global mental health crisis constituted by the high burden of mental disorders and unmet needs for care (Patel *et al.,* 2018). Air pollution could play a part in a complex multi-faceted solution to reduce the burden of these disorders. Therefore, the purpose of the introduction is to establish an understanding of mental health and air pollution as well as the significance of the proposed research question.

1.1 Mental Health and Well-being

1.1.1 Meaning

WHO summarises mental health as a state of mental well-being that enables people to cope with the stresses of life, learn and work well, as well as contribute to their community. It is an integral component of health and well-being that underpins individual and collective abilities to make decisions, build relationships and shape the world (WHO, 2022). Therefore, mental health is more than the absence of mental disorders. It is experienced differently from one person to the next, with varying degrees of difficulty and distress. People with mental health conditions are more likely to experience lower levels of mental well-being, but this is not always or necessarily the case. For example, people with severe mental disorders such as schizophrenia can have good well-being. Consequently, leading to potentially very different social and clinical outcomes (WHO, 2022). Therefore, defining mental health is challenging which is further emphasised by a persistent lack of standardised definitions, stigmatisation, and lack of recognition of mental health in many places (Romanello *et al.,* 2022).

The two classification systems for mental disorders are the International Classification of Disease (ICD-10/11) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). ICD-10 defines a mental disorder as “a clinically recognizable set of symptoms or behaviours associated in most cases with distress and with interference with personal functions” (International Advisory Group for the

Revision of ICD-10 Mental and Behavioural Disorders, 2011). DSM-V uses a similar however more complex definition for example it does not pathologize the human response to loss. The definition highlights a "clinically significant disturbance in an individual's cognition, emotion regulation, or behaviour… that reflects a dysfunction in mental functioning" (Stein *et al.*, 2021). In the UK mental disorder, condition, and illness is often used interchangeably. The most common mental disorders include anxiety disorders and depression which are shown above in **Figure 1.1** (WHO, 2022). Moreover, comorbidity is common amongst these disorders such as experiencing symptoms of anxiety and depression. Other terms such as emotional/psychological well-being or emotional health are also increasingly used to avoid pathologizing the range of human emotions and experiences (Lawrence *et al.,* 2021). **Figure 1.2** below summarises the terms well-being, mental health, and mental illness with examples. In this thesis various types of behaviours and conditions related to mental health with different presentations and severities will be explored (**Table 1.1**).

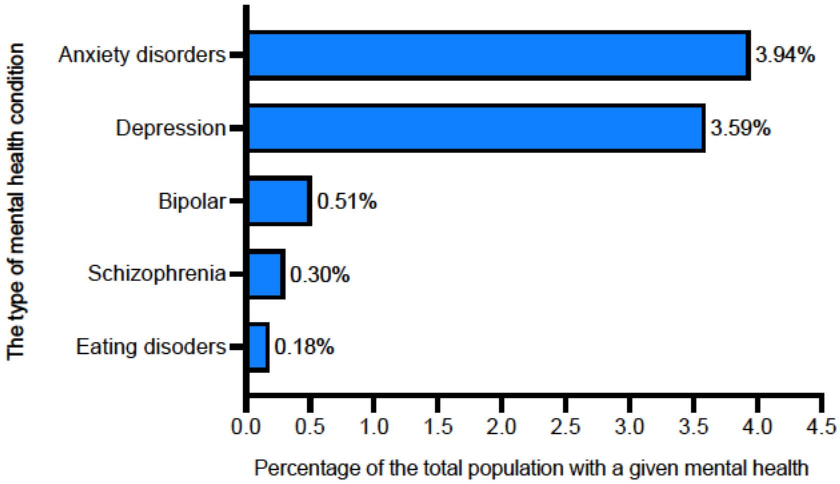

Figure 1.1- The percentage of the global population with anxiety disorders, depression, bipolar, schizophrenia and eating disorders in 2019. The graph was created by EC using data from the Institute for Health Metric and Evaluation's (IHME) Global Burden of Disease (GBD).

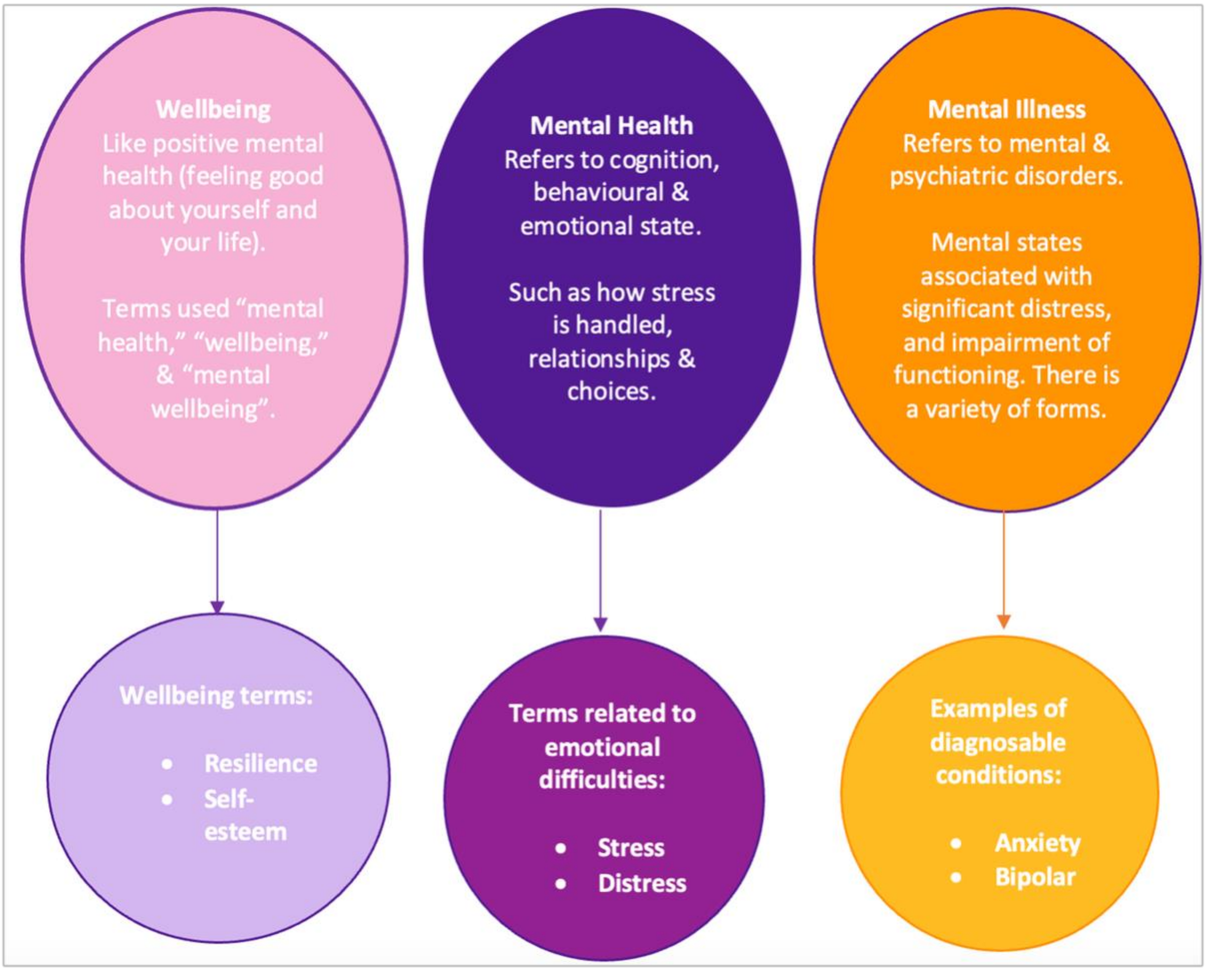

Figure 1.2 - Aims to define the terms well-being, mental health, and mental illness. Huppert and So (2013) described well-being as the same as positive mental health which consists of emotional stability, engagement, optimism, positive emotion, and relationships as well as resilience and self-esteem. Mental health refers to cognition, emotional state, and behaviour for example how individuals cope with stress and the choices they make. Mental illnesses are diagnosed after prolonged mental states associated with significant distress and impairment of functioning (American Psychiatric Association, 2013).

Table 1.1- Summary of behaviours and conditions related to mental health which will be discussed in this thesis.

Terminology	Summary
Emotional stress	Most people will feel stress at some point, and some find stress helpful or motivating. However, when stress is affecting an individual's life it can cause a variety of symptoms: • Physically *e.g.,* headaches, pain, stomach problems, or a faster heartbeat. • Mentally *e.g.,* struggling to make decisions, feeling overwhelmed, constantly worrying, forgetfulness. • Behaviour changes *e.g.,* irritability, excessive sleeping or eating, drinking, or smoking more (NHS, 2022c).
Emotional distress	Is a state of emotional suffering which encompasses a wide range of symptoms similar to emotional stress (Kandola, 2020). However, the main symptoms are anxiety and depression (Kandola, 2020). It can be caused by: • A mental health issue(s). • Or circumstance(s), *e.g.,* relationship difficulties or financial strain. Anyone can experience emotional distress, even if they do not meet the criteria for any psychological disorder (Kandola, 2020).
Adjustment disorders	An unhealthy or excessive emotional or behavioural reaction to a stressful event or change in a person's life within three months of it happening (Carta *et al*., 2009).
Somatoform disorders	When an individual experiences physical symptom(s) such as pain in response to psychological distress or mental health issues (Goodman, 2020).
Depression	A common disorder which affects 3 in 100 people per week. It is characterised by: • Sadness, • Loss of interest or pleasure, • Feelings of guilt or low self-worth,

	• Disturbed sleep or appetite, • Poor concentration, • Physical complaints with no apparent physical cause (WHO, 2022). Depression is particularly serious as it can lead to suicide (WHO, 2022).
Anxiety Disorders	A common disorder which affects 6 in 100 people per week (NHS, 2022a). It is a feeling of unease, such as worry or fear, that can be mild or severe (NHS, 2022a). Most people will feel anxious at some point however some people find their feelings of anxiety hard to control and are more constant which can affect their daily lives (NHS, 2022a). Examples of these disorders are: • **Generalised anxiety disorder (GAD)**- long-term condition that causes individuals to feel anxious about a wide range of situations and issues, rather than one specific event. • **Posttraumatic stress (PTSD)**- caused by distressing and/or frightening events which are often relived by the individual through nightmares and flashbacks (NHS, 2022b). Symptoms may include feelings of: - Isolation, - Irritability, - Guilt, - Problems sleeping, such as insomnia, - Difficulty concentrating (NHS, 2022).
Bipolar Disorder	Affects 45 million people worldwide (WHO, 2022). Typically consists of both mania and depression separated by periods of normal mood (WHO, 2022).
Mania	Consists of elevated or irritable mood, over-activity, rapid speech, and a decreased need for sleep (WHO, 2022).
Affective/mood disorders	The main types include depression, bipolar disorder, and anxiety disorders (Burford, 2022).

Schizophrenia and other psychotic disorders	These are severe disorders that affect 20 million people worldwide (WHO, 2022). WHO described common psychotic experiences as: • **Hallucinations**- hearing, seeing, or feeling things that are not there. • **Delusions**- fixed false beliefs or suspicions firmly held even when there is evidence to the contrary. These disorders can make it difficult for people to work or study normally.
Personality disorder	People with this condition think, feel, behave, and relate to others very differently from the average person (NHS, 2020). Symptoms vary depending on the type: • **Borderline-** (one of the most common types) tends to have disturbed ways of thinking, impulsive behaviour and problems controlling their emotions (NHS, 2020). They may have intense but unstable relationships and worry about abandonment (NHS, 2020). • **Antisocial-** typically get easily frustrated and have difficulty controlling their anger. They may blame others for problems in their life and be aggressive (NHS, 2020).
Eating Disorders	In 2019, 14 million people experienced eating disorders including almost 3 million children and adolescents (Institute for Health Metrics and Evaluation, 2019). Eating disorders, such as anorexia and bulimia nervosa, involve abnormal eating and preoccupation with food as well as prominent body weight and shape concerns (WHO, 2022). The symptoms or behaviours can result in significant: • Risk or damage to health, • Distress, • Impairment of functioning (WHO, 2022).
Self-Harm or non-suicidal self-injury	Refers to any act of intentional self-injury or poisoning regardless of suicidal intent or motivation (Hawton *et al.,* 2012).
Suicide	Is mortality caused by injuring oneself with the intent to die. Occurs throughout the lifespan and is the second-leading cause of mortality in 15- to 29-year-olds worldwide, after road injury (WHO 2021).

Suicide Ideation	Often called suicidal thoughts or ideas, is a broad term used to describe a range of contemplations, wishes, and preoccupations with death and suicide (Harmer *et al.,* 2022). However, there is no universally accepted consistent definition (Harmer *et al.,* 2022). Suicide ideation and attempts are strongly predictive of suicide mortality (Klonsky *et al.,* 2016).

Dementia and developmental disorders are also classified in ICD-10 under the umbrella term mental and behavioural disorders. These conditions are summarised, and their clinical outcomes explained in **Table 1.2**. The effect of air pollution on these disorders will not be investigated in this review.

Table 1.2- Summary of dementia and developmental disorders which will not be discussed in this thesis.

Terminology	**Summary**
Dementia	Effects approximately 50 million people globally (WHO, 2022). It is usually chronic or progressive where deterioration in cognitive function is beyond what might be expected from normal ageing (WHO, 2022). Memory, thinking, comprehension, learning capacity, language, and judgement are affected (WHO, 2022). Impaired cognition is commonly accompanied, by deterioration in emotional control, social behaviour, or motivation (WHO, 2022).
Developmental Disorders	Umbrella term covering intellectual disability and conditions such as autism. Developmental disorders usually begin in childhood and persist into adulthood, causing impairment or delay in functions related to the central nervous system (CNS) maturation (WHO, 2022). Unlike mental disorders which often consist of periods of remission and relapse, developmental disorders generally follow a steady course (WHO, 2022).
Intellectual disability	Characterised by impairment of skills across multiple developmental areas such as cognitive functioning and adaptive behaviour (WHO, 2022). Lower intelligence decreases the ability to adapt to the variability in life (WHO, 2022).
Autism	Involves impaired social behaviour, communication and language, and a narrow range of interests and activities that are both unique to the individual and are

	carried out repetitively (WHO, 2022). People with these disorders could display some degree of intellectual disability (WHO, 2022).

1.1.2 Prevalence and Burden of Mental Disorders

Mental disorders remain widely under-reported, and there is a scarcity of data on their impacts and care provided (Romanello *et al.,* 2022). This is particularly evident in lower income countries where data is scarcer, and there is less attention and treatment for mental health disorders (Romanello *et al.,* 2022). The prevalence figures below are estimates and do not reflect diagnosis data, but are imputed from a combination of medical, epidemiological data, surveys and meta-regression modelling where raw data is unavailable. These estimates are from the Institute for Health Metric and Evaluation's (IHME) Global Burden of Disease (GBD) (Dattani *et al.,* 2021) and were used to create **Figure 1.3** and **1.4**.

One in every eight people, or 970 million globally, in 2019, were living with a mental disorder (not including alcohol or drug dependence) (**Figure 1.3**) (WHO, 2022). The COVID-19 pandemic, in 2020, caused an estimated 26% and 28% increase respectively for anxiety and major depressive disorders in just one year (WHO, 2022). There are approximately 4.6 million people with mental disorders in the UK (not including alcohol and drug use disorders) (Dattani *et al.,* 2021). This equates to roughly one in four adults (Watkins, 2022). In the most deprived areas of Wales 20% of people report being treated for a mental health condition compared to 8% in the least deprived areas (Watkins, 2022).

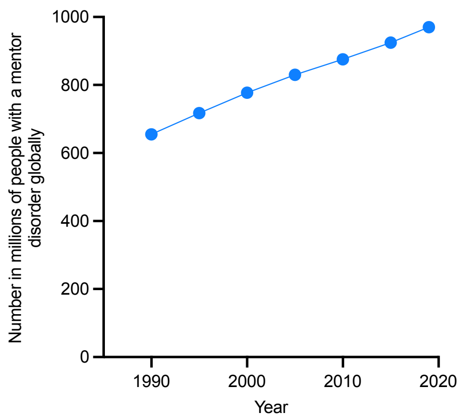

Figure 1.3- The increase in mental and developmental disorders globally from 1990-2019. Age was standardised.

The overall burden of disease is assessed using the disability-adjusted life year (DALY), a time-based measure that combines years of life lost due to premature mortality (YLLs) and years of healthy life lost due to disability (YLDs) (Dattani *et al.,* 2021). One DALY represents the loss of the equivalent of one year of full health (Dattani *et al.,* 2021). Mental and substance use disorders account for around 5% of global disease burden and are ranked 7th highest DALY. In the UK, mental disorders account for 7% of the disease burden which is the 4th highest DALY shown in **Figure 1.4** below. Current predictions indicate that by 2030 depression will be the leading cause of disease burden globally (WHO, 2011).

The global burden of disease attributable to mental disorders has risen in all countries in the context of a diverse range of major demographic, environmental, and socio-political transitions (**Figure 1.3**) (Patel *et al.,* 2018; WHO, 2023c). Therefore, the investigation of environmental variables such as air pollution with consideration of demographic and socioeconomic variables is vital to help develop resolutions. This is emphasised further since the quality of mental health services is routinely worse than the quality of those for physical health (Patel *et al.,* 2018). Furthermore, government investment and development assistance for mental health remains small (Patel *et al.,* 2018). Collective failure to respond to this global health crisis results in monumental loss of human capabilities and avoidable suffering (Patel *et al.,* 2018). Therefore, understanding the aetiology of mental disorders and potential modifiable factors such as air pollution is paramount.

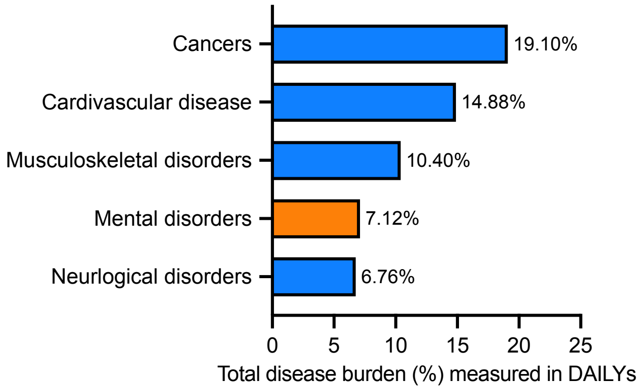

Figure 1.4- The share of total non-communicable disease burden by cause in the UK (2019).

1.1.3 Aetiology of Mental Disorders

Despite the prevalence of mental disorders, their aetiology is largely unknown (Misiak, 2020). Since, many of the potential risk factors for mental health conditions remain only correlates. However, it is likely to involve a complex interaction between different biopsychosocial (biological, psychological, and socio-environmental) risk factors (WHO, 2012; Misiak, 2020; Dattani *et al.,* 2021):

- **Individual attributes and behaviours:** these can be genetic factors or personality traits such as low self-esteem, medical illness, and substance abuse.
- **Social and economic circumstances:** low income and poverty, neglect, family conflict, and work stress.
- **Environmental:** injustice and discrimination, social and gender inequalities and exposure to war or disaster.

The risk factors and influencers on mental health vary for an individual as they move through the life-course. For example, in the pre-conception and pre-natal period, detrimental behaviours include tobacco use, alcohol and drug use which can increase the likelihood of later mental health disorders (Dattani *et al.,* 2021). Identifying modifiable risk factors for illness onset, severity and relapse is a crucial research challenge. Since this could reduce the human suffering and high economic costs caused by long-term chronic mental illness. One potential modifiable risk factor is air pollution/quality.

1.1.4 Defining Mental Health in Research and the Challenges

Another research challenge is defining mental health which has often been regarded as more difficult than measuring other types of health (King, 2018). This is partly due to psychiatry's limited availability of objective biological tests and variable diagnostic guidelines, alongside intercultural differences in the mental health experience and complex social as well as psychological confounders (King, 2018). In research mental health can be assessed in various ways:

1. **Gathering existing data** such as diagnoses, health history, prescription information, referrals, psychologist attendance, or police records. In addition to participants self-reporting their own psychiatric diagnoses or medications which is used regularly instead of specific assessment tools (King, 2018).
2. **Biological measurement:** most notably electroencephalogram (EEG) brainwave monitoring, or salivary cortisol as proxy measures of stress levels (King, 2018).
3. **Diagnostic interview:** by trained clinicians, such as a psychiatrist or clinical psychologist.
4. **Screening assessment tools:** shorter interviews or self-completed questionnaires such as Patient Health Questionnaire 9 (PHQ-9), and General Anxiety Disorder 7 (GAD-7) which are frequently used in research as indicators of symptoms of depression and anxiety to assess mental health (Stocker *et al.,* 2021).

The gold standard for defining mental health is the diagnostic interview using ICD or DSM guidelines as it is a definitive measure of an individuals' mental health (Kiely & Butterworth, 2015). However, urban design research normally involves examining the effects of environmental exposures on sizeable populations (King, 2018). Therefore, it is often not feasible to employ enough psychiatrists or psychologists to assess many people in this manner. Due to the challenges of conducting rigorous psychiatric interviews such as scale, time and resources for large populations, screening tools have been developed with the aim of more efficiently assessing specific components of mental health (King, 2018). These tools have nearly just as much accuracy as diagnostic interviews (King, 2018). Furthermore, they are often much shorter interviews, which can be competently delivered by anybody after just a few sessions of training (King, 2018). Another screening tool are self-completed questionnaires which can be used to target specific geographical areas, or demographic groups of interest. These tools can also generate a continuous variable instead of discrete clinical diagnoses. Defining mental health is not just a challenge in research settings but also in clinical settings.

1.1.5 Diagnosing Mental Disorders and the Challenges

There are two major diagnostic manuals which are the authoritative guidebooks for medical professionals and specific research applications to use for the diagnosis, classification, and treatment of mental disorders (Clark *et al.,* 2017). The two major diagnostic manuals are:

1. **International Classification of Diseases (ICD)**- internationally recognised and maintained as well as published by WHO (WHO, 2023b). This includes information on all morbidity and mortality.
2. **Diagnostic and Statistical Manual of Mental Disorders (DSM)**- primarily for the United States and published by the American Psychiatric Association (APA). It is used by clinicians and researchers to diagnose and classify only mental disorders.

Despite the publication of these diagnostic manuals and the increase in knowledge during the past half century on mental disorders, the understanding of their components and processes remains rudimentary (Clark *et al.,* 2017). Since, understanding and classifying mental disorders has many challenges:

1. **Aetiology**: is unknown but is likely to involve multiple factors (Clark *et al.,* 2017).
2. **Categorisation**: due to the multidimensional nature of mental disorders. For example, varying degrees of severity, co-occurring symptoms between disorders and multiple subtypes (Clark *et al.,* 2017).
3. **Thresholds**: which set the boundaries between disorder, severity, and no disorder. These are difficult to define as the definition of a mental disorder remains a subject of debate as mentioned previously (Telles-Correia *et al.,* 2018). Furthermore, deciding if the symptoms presented are sufficiently intense or persistent enough to be considered disordered is subjective (Clark *et al.,* 2017).
4. **Comorbidity**: individuals with mental illness often meet diagnostic requirements for multiple conditions (Clark *et al.,* 2017).

Therefore, these complexities add to the challenges of research involving mental disorders.

1.1.6 Self-reporting of Mental Health and the Limitations

Another method of collecting mental health data in research is using self-reports. In psychology, a self-report is any test, measure, or survey that relies on an individual's own report of their symptoms, behaviours, beliefs, or attitudes (Salters-Pedneault, 2023). This data is gathered typically from paper-and-pencil or electronic format, or sometimes through an interview (Levin-Aspenson & Watson, 2018). Self-report data is commonly used in psychological studies as it can be:

- Easy to obtain
- Inexpensive
- Performed relatively quickly, to obtain results in days or weeks rather than observing a population over the course of a longer time frame.
- Made in private and can be anonymized to protect sensitive information and perhaps promote truthful responses (Warner *et al.,* 2011).
- Used to reach more subjects than could be analysed by observation or other methods (Salters-Pedneault, 2023).

However, collecting information through self-reporting has limitations:

- **Honesty**: People are often biased when they report on their own experiences (Devaux & Sassi, 2015). Subjects may make the more socially acceptable answer consciously or unconsciously rather than being truthful (Salters-Pedneault, 2023).
- **Introspective ability**: The subjects may not be able to assess themselves accurately (Salters-Pedneault, 2023).
- **Interpretation of questions**: The wording of the questions may be confusing or have different meanings to different individuals (Salters-Pedneault, 2023).
- **Rating scales**: Rating something yes or no can be too restrictive, but numerical scales can be inexact and subject to individual inclination to give an extreme or middle response to all questions (Salters-Pedneault, 2023).
- **Response bias**: Questions are subject to biases from previous responses and whether they relate to recent or significant experiences and other factors (Salters-Pedneault, 2023).
- **Sampling bias**: Some people may be more likely to complete questionnaires than others. Therefore, there could be bias towards a certain type of person who has, for example, the time to complete questionnaires which may not be representative of the population being studied (Salters-Pedneault, 2023).

Most experts in psychological research and diagnosis suggest that self-report data should not be used alone, as it can be biased (Althubaiti, 2016). Research could be more accurate when self-report data is combined with other information, such as an individual's behaviour or physiological data. This "multi-method" assessment provides a more global, and therefore likely more accurate, picture of the subject. It is also important that the questionnaires used in research are checked to see if they produce consistent results over time and are validated by another data method (Hopwood *et al.,* 2018). This helps demonstrate that responses measure what they claim they measure (Hopwood *et al.,* 2018). The advantage of validated scales such as GAD-7 in research is that it means the same mental health outcome can be measured across various studies. Therefore, defining mental health in research is a challenge adding to the complexities of investigating the association between mental health and air pollution.

1.2 Air Pollution and Air Quality

1.2.1 Definition

Air pollution can be defined as a complex mixture of carbonaceous and transition metal particulates, endotoxin, pollens, gases (*e.g.,* NO_2, O_3, CO_2) as well as various chemical vapours (Almetwally *et al.,* 2020). One of the major constitutes of air pollution is, Particulate Matter (PM), a broad term for microscopic particles suspended in air originating from a range of human-made and natural sources (Blake & Wentworth, 2023). Common sizes which can be inhaled are: PM_{10} particles with diameters that are generally smaller or equal to 10 micrometres; and $PM_{2.5}$, ultrafine particles, with diameters that are generally smaller or equal to 2.5 micrometres (Almetwally *et al.,* 2020). Nitrogen dioxide (NO_2) is one of a group of gases called nitrogen oxides (NO_x) (Blake & Wentworth, 2023). Nitric (NO) emissions are produced from fossil fuel combustion *e.g.,* road transport and react atmospherically to produce NO_2, which is also directly emitted (Blake & Wentworth, 2023). Pollution can come in two different types: indoor and outdoor. Some examples of indoor pollution are smoke from cooking, heating, social habits, infrastructure, and cleanliness. Examples of outdoor pollution are vehicles, power generation, agriculture/waste incineration, and industry (Almetwally *et al.,* 2020).

Air quality describes how polluted the air is. One method of measuring this is the Air Quality Index (AQI) (2022) which is based on the measurement of $PM_{2.5}$ and PM_{10}, ozone (O_3), NO_2, sulphur dioxide (SO_2) and carbon monoxide (CO) emissions around the world. Categories according to AQI are:

- **0-50** is good air quality which poses little to no risk to health.
- **51-100** is moderate air quality which is acceptable. However, for some pollutants there may be a moderate health concern for a very small number of people who are usually sensitive.
- **101-150** is unhealthy for sensitive groups but the public is unlikely to be affected.
- **151-200** is unhealthy for everyone who may begin to experience health effects with members of sensitive groups potentially experiencing more serious consequences.
- **201-300** is very unhealthy and the entire population is more likely to be affected.
- **300+** hazardous to all who could experience serious health effects.

The effects of exposure to reduced air quality and increased air pollutant concentrations on mental health will be explored in this thesis.

1.2.2 Exposure Assessment

Human exposure assessment usually describes how an individual or population encounters a contaminant such as air pollutants (Zhang & Lioy, 2002). This includes quantification of air pollution across space and time, for individuals and populations (Zhang & Lioy, 2002). Understanding the effects of air pollution on health involves:

1. Source
2. Concentration
3. Exposure
4. Dose
5. Adverse effects

Exposure, the contact between air pollutants and a target, is the key to linking the pollution source (chemical or biological contaminant) and health effects (Zhang & Lioy, 2002). Human exposure to air pollutants depends on exposure concentration and duration (Zhang & Lioy, 2002).

Exposure can be quantified using different methods:

1. **Direct air monitoring (exposure assessment)**- measures exposures directly using personal monitors, indoor-outdoor sampling, and mobile monitoring (Han *et al.,* 2017).
2. **Indirect air monitoring (exposure assessment modelling)**- predicts exposure using models to combine activity pattern data with microenvironmental concentration data (Duan & Mage, 1997). Examples, fixed-site monitors combined with data on time-activity patterns, proximity models, interpolation models, air dispersion models, and land-use regression (LUR) models (Han *et al.,* 2017).

Both methods have advantages and limitations. Despite the simplicity of personal monitors and higher spatiotemporal resolution due to capturing personal air quality information, personal monitors, are costly and vulnerable to sample selection bias (Duan & Mage, 1997; Xie *et al.,* 2021). Since, usually personal monitors impose a substantial burden on the respondents (Duan & Mage, 1997; Xie *et al.,* 2021). This can make it difficult to recruit a representative sample (Duan & Mage, 1997). Whereas indirect monitoring is lower in cost and imposes less respondent burden, thus is less vulnerable to sample selection bias and large populations can be studied (Duan & Mage, 1997). Furthermore, personal monitors have reduced accuracy compared to regulatory or research-grade monitors (Xie *et al.,* 2021). Therefore, air pollution exposure estimates for research studies are often based on measurements taken by stationary regulatory monitors (Xie *et al.,* 2021). While these monitors are highly accurate and well-suited for ensuring compliance to federal air quality standards, their utility for capturing individual-level pollution exposure is limited (Xie *et al.,* 2021). Due to the relative sparsity of monitor locations, they rarely coincide with the locations that exposure takes place (*e.g.,* home, work, or school) (Zhang & Lioy, 2002; Xie *et al.,* 2021). Therefore, an individual's exposure to air pollution can be measured indirectly through spatial interpolation techniques, such as inverse distance weighted interpolation and kriging, or statistical methods, such as land-use regression (LUR) modelling (Xie *et al.,* 2021).

Indirect methods of exposure assessment also typically estimate exposure for a single location per individual, such as their residence (Xie *et al.,* 2021). However, this does not capture exposures that occur at different locations or during regular activities like commuting and errands (Xie *et al.,* 2021). Furthermore, regulatory monitors offer limited temporal resolution (*e.g.,* hourly averages in the case of PM monitors), which may lead them to miss transient spikes in pollution levels. Methods that rely on outdoor regulatory monitors can only capture *ambient* pollution concentrations rather than exposures occurring inside the home or other indoor settings (Xie *et al.,* 2021). This is a significant limitation given most individuals in industrialized nations spend >90% of their time indoors (Klepeis *et al.,* 2001; Choi *et al.,* 2020). Additionally, results from many exposure studies indicate that people are likely to receive the greatest exposure to many toxic air pollutants not outside but in indoor settings (Zhang & Lioy, 2002). Consequently, accurately measuring air pollution exposure as well as mental health outcomes in research can be challenging. Further, adding to the complexities of investigating the association between air pollution and mental health. Therefore, recommendations for the quantification of air pollution are important.

1.2.3 Committee on the Medical Effects of Air Pollutants (COMEAP) Recommendations

COMEAP advises the government on all matters concerning the health effects of air pollutants. Some of the COMEAP recommendations for the quantification of the health effects associated with air pollutants are:

- Estimate the burden attributable to the whole pollution mixture.
- Coefficients for the same health effect associated with $PM_{2.5}$ and PM_{10} should not be used together in the same assessment.
- Associations for short- and long-term exposure for the same pollutant are not combined for the same health endpoint.

The use of single pollutants is not recommended due to uncertainties around the effects of individual pollutants on health and concentrations of pollutants are often correlated (COMEAP, 2020). Combining the coefficients for $PM_{2.5}$ and PM_{10} is not recommended since $PM_{2.5}$ is part of PM_{10}. Therefore, the exposure-response coefficients derived by analysing PM_{10} may be applicable for fine particles also and coefficients from analysing $PM_{2.5}$ may also include coarse particles (COMEAP, 2020). Combining short- and long-term exposure associations between the same pollutant and a mental health outcome is not recommended (COMEAP, 2020). Since there may be overlaps from the effects of short-term exposure when investigating long-term exposure and the other way round (COMEAP, 2020). Understanding the recommendations for quantifying the health effects of air pollutants on mental health is essential when deciding on the quality of studies and for future research.

1.2.4 Effects of Air Pollution on Human Health

The physical effects of air pollution are well researched and reported upon compared to the mental health consequences. An estimated 7 million people worldwide die every year from increased air pollution/decreased air quality (WHO, 2021). Ambient $PM_{2.5}$ was the fifth-ranking mortality risk factor in 2015 and caused 7.6% of total global deaths (Cohen *et al.,* 2017). Consequently, air pollution is considered the single biggest environmental threat to human health, alongside climate change (WHO, 2021). Particularly, as most of the world's population (99%) continue to be exposed to levels of air pollution substantially above WHO Air Quality Guidelines (AQG) (Shaddick *et al.,* 2020; WHO, 2021). Furthermore, despite efforts to reduce air pollution in many countries there are regions, especially Central and Southern Asia as well as Sub-Saharan Africa, where populations continue to be exposed to increasing levels of air pollution (Cohen *et al.,* 2017; Shaddick *et al.,* 2020). Since WHO's last 2005 global update, there has been a marked increase of evidence that shows how air pollution affects different aspects of health (WHO, 2021). For that reason, and after a systematic review of the accumulated evidence, WHO has recommended reduced levels for PM, O_3, NO_2, SO_2 and CO in 2021 (WHO, 2021).

Inhalation of polluted air is the cause of a wide range of physical health effects. The air pollutants, PM, NO_2 and O_3 are of the most concern for human health in urban areas (Blake & Wentworth, 2023). No safe lower limit has been identified for these pollutants, which disproportionately affect vulnerable groups (Blake & Wentworth, 2023). Examples of these vulnerable groups are the elderly, children, people living with pre-existing health conditions and in poverty (United Nations Environmental Programme, 2018; Manisalidis *et al.,* 2020).

The short-term effects of air pollution, which are temporary, can cause pneumonia or bronchitis as well as discomfort such as irritation to the nose, throat, eyes, or skin (Almetwally *et al.,* 2020). The long-term effects can last for years or an entire lifetime and result in mortality. These effects include cardiovascular and respiratory disease as well as lung cancer (Cohen *et al.,* 2017; Almetwally *et al.,* 2020). The International Agency for Research on Cancer (2013) has classified air pollution, especially $PM_{2.5}$, as a leading cause of cancer. It is estimated 500,000 lung cancer deaths and 19% of cardiovascular deaths can be attributed to air pollution (Schraufnagel *et al.,* 2019). Additionally, WHO provides evidence of links between exposure to air pollution and type 2 diabetes, obesity, and systemic inflammation (WHO, 2015). A recent global review even found that chronic exposure can affect every organ in the body, complicating and exacerbating existing health conditions (Schraufnagel *et al.,* 2019; National Geographic, 2021).

However, the effects on the CNS are only starting to be widely recognised (Buoli *et al.,* 2018). Some studies have found a link between air pollution and cognitive decline which can, potentially, progress to dementia (Chen *et al.,* 2017; Schikowski & Altuğ, 2020). In addition to associations between various mental disorders and air pollution (Buoli *et al.,* 2018; Braithwaite *et al.,* 2019). There is, however, a lack of high-quality literature considering the effects of air pollution on mental health (Gladka *et al.,* 2018; Braithwaite *et al.,* 2019). Despite, guidelines from reports encouraging parity of esteem between physical and mental health (Panday, 2016). Since mental health problems significantly increase the risk of physical health problems (and *vice versa*) (Ohrnberger *et al.,* 2017). Therefore, mental health consequences could be a secondary outcome of poor physical health or *vice versa*. Since, it has been shown mental illness increases the risk of premature mortality due to cancer, heart disease, lung disease and obesity related conditions (Thornicroft, 2011; Iturralde *et al.,* 2021). Moreover, children with mood disorders were more susceptible to adverse physiologic effects of air pollution compared to those without (Dales & Cakmark, 2016). Therefore, consideration of both physical and mental health is necessary to reduce the burden of pollution induced disease and the consequences to human health.

1.3 The link between Mental Health/Well-being and Air Pollution

The link between mental health and air pollution requires a closer examination. In this section the potential mechanisms linking air pollution and mental health will be discussed. These mechanisms involve the ability of air pollutants to translocate to the brain which may cause inflammation, blood brain barrier dysfunction, and oxidative stress. These physiological processes have also been linked to mental disorders. Additionally, high air pollution levels in relation to climate change and urbanisation will be discussed. Finally, in this section the current research and limitations on the association between air pollution and mental health will be explored.

1.3.1 Translocation of Air Pollutants to the Brain

Exposure to pollutants may affect the CNS and brain health, contributing to increased risk of cognitive dysfunction, depression, and other psychiatric disorders (Hahad, 2020). Evidence suggests inhaled ultrafine particles (UFP) and constituents can translocate to the brain (**Figure 1.5** below) (Oberdörster *et al.,* 2008). Initially, particles are deposited in the upper and lower airways and reach the lung as well as the gastrointestinal tract (Peters, 2023). The UFP and constitutes can then gain access to the brain in multiple ways:

1. Mainly directly from the nasal cavity via the olfactory nerve (**Figure 1.5:1**) (Oberdörster *et al.,* 2008; Oberdörster *et al.,* 2009; Lucchini *et al.,* 2012; Peters, 2023).
2. Via translocation from the lung or the gastrointestinal tract to the bloodstream which is less common (**Figure 1.5:2**) (Oberdörster *et al.,* 2009; Lucchini *et al.,* 2012; Peters, 2023).

It has been demonstrated by experimental studies that UFP are able to pass the blood–brain-barrier (Heusinkveld *et al.,* 2016). UFP have been detected along with evidence for neurovascular damage in several brain regions using imaging modalities such as transmission electron microscopy (Peters, 2023). Furthermore, inflammatory processes induced by $PM_{2.5}$ in multiple barrier organs could result in systemic oxidative stress and inflammation. These are common features of air pollutant-induced disease processes which will be discussed further below (Thomson, 2019; Hahad *et al.,* 2020).

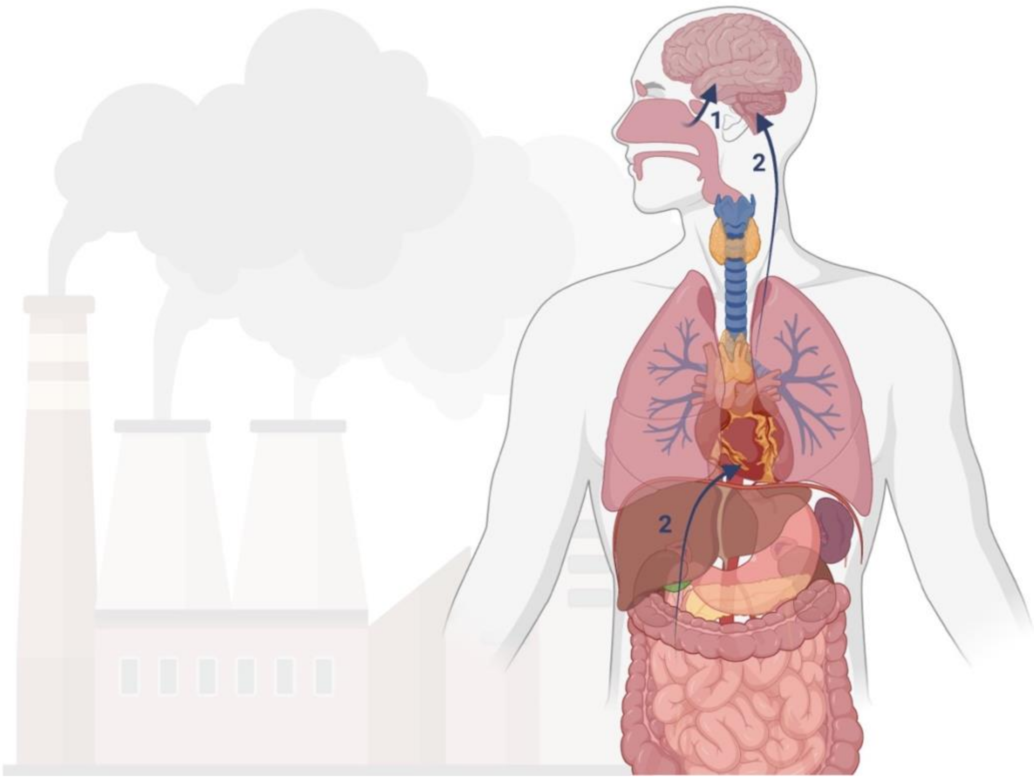

Figure 1.5 - Demonstrates how air pollutants translocate to the brain. The main route is labelled one. **1)** Directly from the nasal cavity. **2)** Via translocation from the lung or the gastrointestinal tract to the bloodstream. The diagram was created with BioRender.com.

1.3.2 Inflammation and the Blood-brain-barrier (BBB) Dysfunction

The molecular mechanisms of causality for the association between air pollution and mental health are unknown (Misiak, 2020; Bakolis *et al.,* 2021). Despite, evidence airborne pollutants can access the brain, and cause inflammation as well as oxidative stress which are common features of psychiatric disorders (Thomson, 2019; Hahad *et al.,* 2020). Air pollutants have been shown to cause inflammation and altered cerebral microvascular integrity in the brain of mice increasing the permeability of their blood brain barrier (BBB) (Milani *et al.,* 2020; Adivi *et al.,* 2021). Inflammation has also been shown to be a mediating pathway to onset, risk, as well as the neuro-progression of depression and other psychiatric disorders (Berk *et al.,* 2013; Beurel, Toups, & Nemeroff, 2020). Moreover, BBB associated tight junction disruption and dysregulation is a suggested common pathology of psychiatric disorders (Pollak *et al.,* 2017; Greene *et al.,* 2020). The dysregulation of the BBB in individuals with mental health conditions could cause increased permeability to ultrafine particles as well as inflammatory markers (Oberdörster *et al.,* 2009; Pollak *et al.,* 2017). This could result in the exacerbation or onset of mental health conditions. Although, ultimately, the potential links between air pollution, increased permeability of the BBB, inflammation and psychiatric disorders has yet to be explored.

1.3.3 Inflammation, Hypothalamic-Pituitary-Adrenal (HPA) Dysfunction and Chronic Stress

Inflammation, dysregulation of the HPA axis and chronic stress are also physiological processes that could explain the potential association between air pollution and mental health. Recent experimental evidence has shown that air pollution, can activate the HPA axis and release cortisol (stress hormones) as part of a neuroendocrine stress response (Li *et al*; 2017; Hajat *et al.,* 2019; Thomson, 2019; Thomson *et al.,* 2021). The brain is highly sensitive to stress, which can affect cognition and mental health, particularly chronic stress which can produce profound biochemical and morphological changes in the brain (Thomson, 2019). Moreover, the morphological alterations due to chronic stress are like those found in the brains of depressed patients examined post-mortem (Mariotti, 2015; Mehta *et al.,* 2018). Chronic stress is also associated with low grade inflammation which is the chronic production of pro-inflammatory factors that may arise from persistent stressors to the body, including increased oxidative and psychosocial stress (Rohleder, 2014; Kim *et al.,* 2020). Chronic activation and/or dysfunction of the HPA axis also increases the burden on physiological stress response systems (Thomson, 2019). It is proposed that the peripheral immune system can interact with the neurocircuitry involved in emotion regulation and behaviour, which may influence the onset of various neuropsychiatric disorders (Irwin & Cole, 2011; Haroon *et al.,* 2012). Chronic low-grade inflammation is not only a possible prelude to psychiatric conditions such as anxiety but also cardiovascular dysfunctions, cancer, and autoimmune syndromes (Furman *et al.,* 2019). Therefore, low-grade systematic inflammation and alterations in the brain caused by chronic stress could potentially provide a mechanism for the association between air pollution and mental health (Mariotti, 2015; Kim *et al.,* 2020).

1.3.4 Urban Environment and Green Space

Urbanisation, the mass movement of populations from rural to urban settings, affects mental health through social, economic, and environmental factors such as air pollution (Srivastava, 2009; Ventriglio *et al.,* 2020). In 2019, the United Nations estimated more than half the world's population (4.2 billion people) live in urban areas, which is expected to increase to 6 billion by 2041. Consequently, more people could be exposed to increased air pollution levels which are positively associated with higher urbanisation (Liang & Gong, 2020; Zhan *et al.,* 2022). Furthermore, the risk of mental disorders is generally higher in more urbanised areas compared to less urbanised or rural areas (Gruebner *et al.,* 2017; Klompmaker *et al.,* 2019; Lauwers *et al.,* 2020; Ventriglio *et al.,* 2020). In addition, increasing evidence demonstrates that green space may be a protective factor for psychological well-being, *e.g.,* reduces stress and improves mental health (Beyer *et al.,* 2014; Klompmaker *et al.,* 2019; Kumar *et al.,* 2019; Lauwers *et al.,* 2020). Psychiatric patients had a significantly lower amount of green space in their neighbourhood compared to the general population (Boers *et al.,* 2018). Therefore, individuals exposed to decreased surrounding green and subsequent air pollution as well as traffic noise had higher odds of poor mental health than single exposure models (Klompmaker *et al.,* 2019). However, despite initiatives towards greening cities to mitigate pollution effects, there is little empirical evidence linking these benefits to air pollution reduction by urban vegetation (Kumar *et al.,* 2019). In addition, there is only emerging evidence about the association between urbanization and mental health issues (Lauwers *et al.,* 2020; Ventriglio *et al.,* 2020). This could be because these associations are highly complex, and there are difficulties covering the broad range of influential factors (Lauwers *et al.,* 2020). Overall, social disparities, pollution, and the lack of contact with nature are some of the recognized factors affecting urban mental health (Ventriglio *et al.,* 2020).

1.3.5 Climate Change

Burning fossil fuels which releases carbon dioxide and greenhouse gases into the atmosphere overtime contributes to climate change a secondary effect of air pollution (WHO, 2023a). Climate change refers to large-scale, long-term shift in the planet's weather patterns and average temperatures (Oppenheimer & Anttila-Hughes, 2016). The consequences of climate change are reduced mental health, psychological well-being, and the exacerbation of pre-existing mental health inequalities in marginalised and vulnerable populations (Lawrence & Wong, 2020; Romanello *et al.,* 2022). Climate related natural disasters such as floods, wildfires, and heatwaves are linked to elevated rates of anxiety and mood disorders, acute stress reactions, PTSD, suicide, and suicidal ideation (Bourque & Willox, 2014; Dodgen *et al.,* 2016; Thomson *et al.,* 2018). In addition to decreased sense of identity from loss of place and grief reactions (Bourque & Willox, 2014; Dodgen *et al.,* 2016; Thomson *et al.,* 2018). Furthermore, droughts can disrupt agricultural production, resulting in scarcity of resources and economic hardship which increases stress and negatively impacts mental health (Obrien *et al.,* 2014; Vins *et al.,* 2015). The impact of climate change and global warming has given rise to emerging psychological concepts, such as eco-anxiety, and ecological grief (Romanello *et al.,* 2022). Eco-anxiety is when the threat of climate change exacerbates mental distress, particularly among young people, even for individuals who are not directly affected (Clayton *et al.,* 2017). Defined by the APA as: “the chronic fear of environmental doom” (Clayton *et al.,* 2017). Ecological grief is felt in relation to experienced or anticipated ecological losses (Lawrence *et al.,* 2021). The interaction between climate change and mental health is complex as it involves diverse and individual factors. Consequently, air pollution and climate change, and the synergies between them, are a threat to individuals and governments due to financial and mental health consequences (Shaddick *et al.,* 2020).

1.3.6 The Current Knowledge and Limitations

Air pollution and its components are associated with various mental health conditions (Buoli *et al.,* 2018; Braithwaite *et al.,* 2019). Regarding increased risk of mental disorders in the short (Li *et al.,* 2020) and long-term (Bakolis *et al.,* 2021) as well as relapse (Newbury *et al.,* 2021). Much of the literature has focused on depression. Literature reviews have found long-term exposure to $PM_{2.5}$ was associated with increased risk of onset of depressive symptoms (Buoli *et al.,* 2018; Braithwaite *et al.,* 2019; Borroni *et al.,* 2021; Liu *et al.,* 2021). While increased concentrations of NO_2 potentially exacerbated symptoms of depression (Buoli *et al.,* 2018). Moreover, Yang *et al*. (2023) found even low levels of air pollutants in the long-term were associated with increased risk of depression and anxiety. It has also been hypothesized that air pollution may increase the risk of schizophrenia and other psychotic disorders (Attademo *et al.,* 2017). This is further supported by evidence that adolescents exposed to the highest annual levels of air pollution reported higher rates of psychotic experiences than those exposed to lower levels (Newbury *et al.,* 2019; Bakolis *et al.,* 2021). Urban air pollution concentration was also associated with an increased risk of emergency department visits for adolescents and young adults with diagnosed mental health disorders (Szyszkowicz *et al.,* 2020). However, a study showed neither CO nor NO_2 were associated with emergency department visits for mental health conditions except substance abuse (Thilakaratne *et al.,* 2020). Furthermore, air pollution was found to only be indirectly associated with mental health (Dzhambov *et al.,* 2018). Overall, findings from the studies so far are inconsistent (Zijlema *et al.,* 2016; Petrowski *et al.,* 2019). Variations in these associations could be due to different pollutants, exposure times and mental health conditions (Pun *et al.,* 2017; Buoli *et al.,* 2018; Braithwaite *et al.,* 2019; Klompmaker *et al.,* 2019). Therefore, a systematic approach associating mental health, pollutants and exposure times is necessary to understand the impact of air pollution on mental health.

Inconsistent findings may also be due to research limitations (Zijlema *et al.,* 2016; Petrowski *et al.,* 2019). Only a few studies benefit from large sample sizes or nationally representative data (Zijlema *et al.*, 2016; Klompmaker *et al*., 2019; Petrowski *et al.,* 2019). Furthermore, findings from population-based studies of mental health are often limited by:

1. Simplicity of brief screening instruments or proxy measures (*e.g.,* prescription of medication) (Oudin *et al.,* 2016; Klompmaker *et al.,* 2019) which lack validity.
2. Over-simplified estimates and surrogates for air pollution exposure (*e.g.,* proximity to major roads) lacks the accuracy of more individual level exposure (Chen *et al.,* 2017).

3. Lack of studies measuring longitudinal exposures to a range of air pollutants from multiple sources (Pedersen *et al.,* 2004).
4. Not controlling for potential confounders, especially urbanisation and deprivation as well as the large number of confounders (Bernardini *et al.,* 2019).

As emphasized previously consideration of deprivation is important as communities of low socioeconomic status tend to live close to heavy traffic (Pratt *et al.,* 2015) and are at higher risk of developing mental health disorders (Reiss *et al.,* 2019). The heterogeneity of methods, different exposure times, various pollutants, and the complex aetiology of mental health conditions results in research difficulties (Braithwaite *et al.,* 2019. For example, proving causality, ambiguity, and questions about the robustness of results (Buoli *et al.,* 2018; Braithwaite *et al.,* 2019). Therefore, rigorous methodology to confirm the current evidence base is needed (Buoli *et al.,* 2018).

1.4 Project Rationale

Ubiquitous exposure to air pollution and the high number of mental disorders potentially causes even small increases in risk to result in a substantial public health burden (Thomson, 2019). Despite this, the potential health, and societal costs of poor mental health in relation to air quality are not represented in the WHO report due to limited evidence (Bakolis *et al.,* 2021). Therefore, it is researchers' responsibilities to investigate and understand the health effects to protect and inform governments, health professionals and the public. To achieve this high-quality research is necessary to improve the understanding of the biopsychosocial impacts of air pollution (Petrowski *et al.,* 2021). The knowledge obtained could contribute to evidence for health care policies and interventions (Shaddick *et al.,* 2020). It is then the responsibility of policy makers and governments to regulate air pollution which is difficult to avoid or improve by lifetsyle choices alone (UK Government, 2018). Consequently, holistic health could be improved, and climate pollutants reduced encouraging local economic development (Shaddick *et al.,* 2020). Overall, acknowledgement and inclusion of air pollution as a significant risk factor in official guidelines could assist in the prevention and treatment of mental disorders (Bakolis *et al.,* 2021).

1.5 Aim

To determine, with consideration of demographic factors (sex, age, and deprivation), if there is an association between exposure to different sources of air pollution/reduction in air quality and a negative impact upon mental health and well-being.

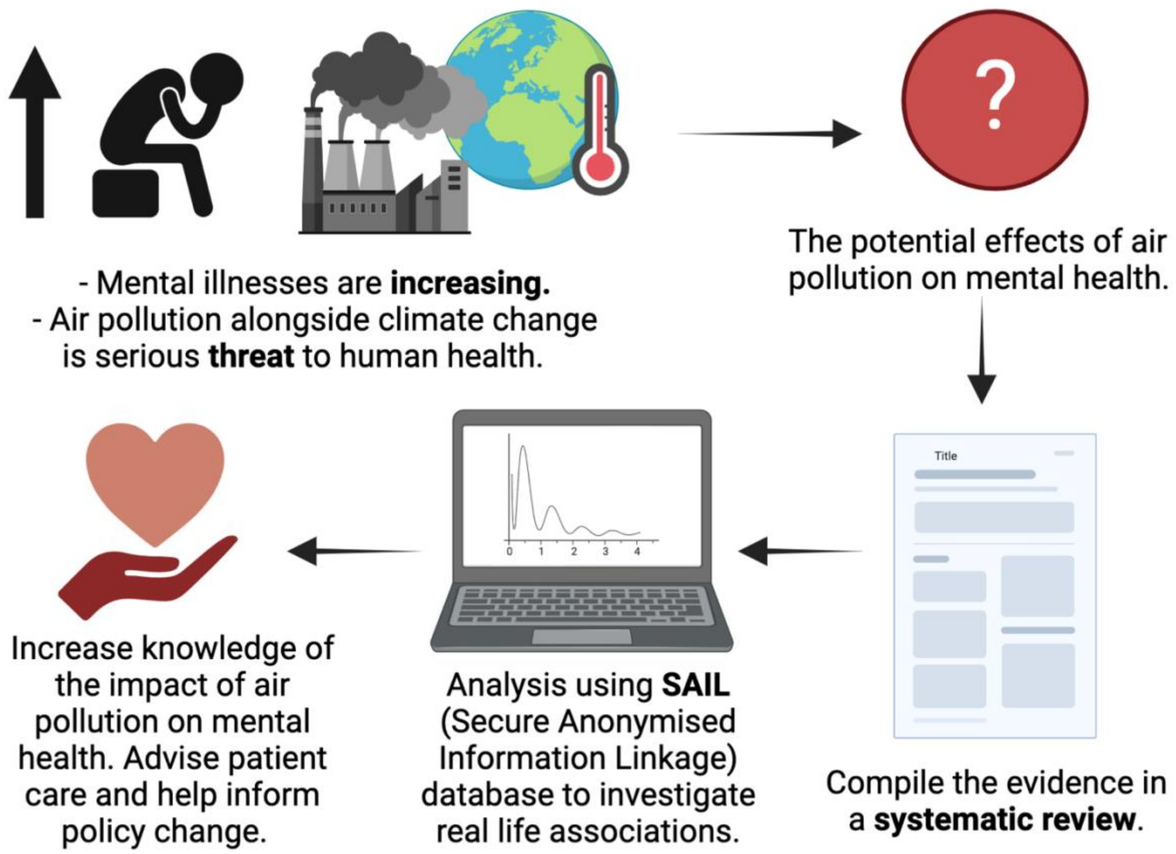

Figure 1.6- Representation of the overview of the project. The first line represents the background and the question for the systematic review. The second line represents the methods and impact of the project.

1.6 Objectives

To achieve the aim, the objectives are as follows which are shown in **Figure 1.6** above:

1. Critical analysis of the literature as part of a systematic review will help assess what is known about the effects of air pollution on mental health, where the knowledge gaps are and any key information. Furthermore, this will lay the foundations for future research in this area.
2. The systematic review will then help identify the mental health outcome and air pollutants to use in the SAIL analysis. This analysis will investigate an association between these two variables and any influence from demographic characteristics.

1.7 Hypothesis

Air pollution is associated to mental health conditions and decreased well-being, which is also affected by demographic variables such as socio-economic status.

Data Chapter 1:

Air Pollution Exposure and Associations with Mental disorders and Wellbeing: A Systematic Review

Declaration: Amy Mizen (AM) and Cynthia Decourcey (CD) assisted in the systematic review methods. CD screened the title and abstract independently and AM resolved any disagreements between EC and CD. AM also quality assessed the data extraction process. Their roles are explained in more detail in section 2.2.

2 Systematic Review

2.1 Introduction

The systematic review aims to identify, evaluate, and summarise the findings from relevant primary studies on the effects of air pollution on mental health issues. Thereby making the available evidence more accessible to decision makers and to help guide clinical practise. Systematic reviews assist in identifying any knowledge gaps to inform research. In this review the statistical associations between various mental health outcomes and air pollutants will be identified. Furthermore, the effects of any demographic variables such as deprivation on this association will also be considered. Therefore, this systematic review will enable the identification of the most appropriate clinical and population data for the linkage of air pollution to general practice (GP) data in the SAIL analysis.

Recent previous systematic reviews have focused on specific clinically diagnosable mental health conditions and/or a certain pollutant (Caspi *et al.,* 2020). Topics of previous systematic reviews are suicide and short-term exposure to air pollution (Davoudi *et al.,* 2021), air pollution and depression (Borroni *et al.,* 2021) and particulate matter with various mental health conditions (Braithwaite *et al.,* 2019). The use of specific mental health conditions does not consider the various dimensions of psychiatric disorders and high rates of simultaneous as well as sequential comorbidity (Caspi *et al.,* 2020). Therefore, for this review, various mental health conditions and well-being issues will be considered, rather than individual psychiatric conditions (Caspi *et al.,* 2020). This could enable an understanding of how air pollution potentially reduces well-being which could eventually result in a mental health diagnosis. To the author's knowledge this is the first systematic review to consider the effects of various pollutants on diagnosed mental health disorders and outcomes below a clinical threshold such as stress.

The aim of this systematic review is to build on the work reported in the above reviews and identify any knowledge gaps. Since previous reviews adopted a narrower scope regarding outcomes and/or timeframes and because additional studies have since been published (Braithwaite *et al.,* 2019).

2.1.1 Aim:

To increase the knowledge and provide a comprehensive understanding of the effects of air pollution on various mental health issues.

2.1.2 Hypothesis:

Specific pollutants will be responsible for the onset/exacerbation of specific mental health conditions.

2.1.3 Objectives:

To achieve the aim, the objectives are as follows:

- Identify relevant literature from a specific time period.
- Summarise and give an overview of the epidemiological evidence, from human studies.
- Evaluate the methodology of the studies to highlight key gaps and limitations in the current research.

2.2 Methods

2.2.1 Population, Exposure, Comparator and Outcome (PECO) Framework

A clearly framed question is vital for conducting systematic reviews and developing health guidance. The PECO framework helps define a research question for a systematic review, assessing the association between exposures and outcomes (Morgan *et al.,* 2018). The terminology in the framework is defined in **Table 2.1**. Therefore, PECO helps define the objectives, informs the study design as well as the inclusion and exclusion criteria (Morgan *et al.,* 2018). Hence, this framework can enable a high-quality systematic review to be conducted.

Table 2.1- Defining PECO

	Definition of the term
Population	The sample that the research is focusing on (Ranganathan, 2019). For example, individuals diagnosed with anxiety.
Exposure	Any factor that may be associated with the outcome of interest. Also called the risk factor/independent variable (Ranganathan, 2019).
Comparator	Investigating changes in the exposure variable (Morgan *et al.,* 2018).
Outcome(s)	Variable that is studied to assess the impact of the exposure on the population (Ranganathan, 2019).

2.2.2 Protocol and Registration

In conducting the systematic review, the Preferred Reporting Items for Systematic reviews, and Meta-Analyses (PRISMA) checklist was followed (Page *et al.,* 2021).

A systematic review protocol was not published beforehand but formulated the following specific research question: "Does exposure to air pollution influence well-being and mental health conditions while considering confounding variables?" according to the PECO framework.

2.2.3 Eligibility Criteria

The PECO framework assisted in determining the inclusion and exclusion criteria to help identify the studies to include and exclude (**Table 2.2**).

Table 2.2- Inclusion and Exclusion Criteria using PECO.

	Inclusion	**Exclusion**
Population	• Humans • Various ages	• Animals • Plants • Individuals with dementia, ADHD, and autism
Exposure	• PM, O_3, NO_2, SO_2, and CO as described by WHO (2021) in their report. • Measurements of PM or UFP concentrations which includes dust. • Defined pollution level. • Any time frame in terms of short or long-term.	• Animals, insecticides, pesticides, and fertilisers • Wildfires • Sea spray and sandstorms due to limited knowledge and studies in this area • Only proxy measures of PM, such as distance from a major road, road density, or traffic intensity or solid air-suspended particles. • Cigarette-related air pollution • Occupational air pollution exposure *e.g.,* firefighters and miners.
Comparator	• Studies comparing risk between individuals exposed to different levels of pollutants. • Baseline well-being.	• Studies without comparison between higher and lower levels of air pollution.

Outcome	• Mental disorders • Suicide and self-harm • Well-being issues • Defined by scientifically accepted symptom based screening, diagnostic instruments, clinical diagnoses (recorded or self-reported), hospital visits, clinic attendance or hospitalization.	• Medication prescribing data as the only outcome. • Not symptom-based measures for the outcome assessment *e.g.,* asking an individual if they have attempted suicide in the last year or someone to rate their stress at a given moment.
Publication type	• Peer reviewed journals.	• Any not subject to peer review process. • Editorials or commentaries which will be used in the discussion.
Study Type	• Primary studies (Philips & Barker, 2021).	• Narrative reviews • Systematic reviews • Meta-analyses (separately identified reference list searching)
Language	• English	• Not English
Publication Date	• 2012- 10th January 2022	• Dates outside of 2012- 10th January 2022
Availability	• Full text	• No full text
Duplicates	• Non-duplicate	• Duplicate

The rationale for the inclusion and exclusion criteria will be explained below.

2.2.4 Inclusion and Exclusion Criteria Rationale

In this systematic review the inclusion and exclusion criteria were broad to help:

- Identify vulnerable groups and any patterns.
- Gain a more comprehensive understanding of the air pollution on various mental health outcomes.
- Investigate the potential impact of demographic variables on possible associations (Centres for Disease Control and Prevention [CDC], 2004).

Depression and pregnancy were excluded after the first full text eligibility screening. Since, more studies were identified than expected which led to concerns around the feasibility of the project. The exclusion criteria and rationale are shown in **Table 2.3** below.

Table 2.3- Rationale for original and updated exclusion criteria

Exclusion Criteria	**Reason(s)**
Dementia, ADHD, and autism	• These conditions involve cognition and learning. • COMEAP (2022) report on dementia and air pollution.
Wildfires	• Stressful event due to threat to life and property. • Not representative of everyday exposure.
Cigarette-related air pollution	• A potential confounding variable as smoking can be used to reduce stress (Choi *et al.,* 2015). • Smoking is common in people with mental disorders (Royal College of Physicians, 2013).
Occupational air pollution exposure.	• Firefighters and miners for example are likely to be exposed to high levels of pollutants.
Medication prescribing data as the only outcome.	• Medication used for mental health conditions can be used for pain, insomnia and ADHD which are not of interest in this study (Braithwaite *et al.,* 2019).

Updated Exclusion Criteria	Reason(s)
Depression	• Recent comprehensive systematic review and meta-analysis on depression and air pollution (Borroni *et al.,* 2021). • Most of the literature focuses on depression and continues to *e.g.,* recent publication by Yang and colleagues (2023).
Pregnancy	• Huge life event which involves many emotions. • Approximately 10% during pregnancy and 13% postnatal experience a mental disorder, primarily depression (Sidhu *et al.,* 2019). • In developing countries this is higher; 15.6% during pregnancy and 19.8% after childbirth (Sidhu *et al.,* 2019). • Particularly vulnerable are women with histories of psychiatric illness who discontinue psychotropic medications during pregnancy (Creeley & Denton, 209).

2.2.5 Information Sources

A systematic search was carried out using the following data bases:

- **PubMed**- primarily MEDLINE journals in the fields of medicine, healthcare systems, and preclinical sciences.
- **PsycINFO**- peer-reviewed literature in behavioural science and mental health.
- **Web of Science**- access to multiple databases that reference cross-disciplinary research, which allows for in-depth exploration of specialised sub-fields within an academic or scientific discipline.
- **Cumulative Index to Nursing & Allied Health Literature (Cinahl)**- literature related to all aspects of nursing, midwifery, and allied health.

Reference lists of eligible reviews and included studies were also screened.

2.2.6 Search Strategy

The last search using the data bases was carried out the 10th January 2022. All databases were searched from inception to present. A combination of relevant index terms and key words were used for air pollution and mental health terminology. Search strategies were modified so that index terms were appropriate to each database used. Citation searches were carried out on the randomly selected studies. Medical Subject Headings (MeSH) terms were used in Cinahl and Pubmed. However, in PsycINfO and Web of Science Mesh terms could not be used. Below are the search terms put into the databases:

Pubmed: "air pollution" [MeSH] OR "air pollutant*" [MeSH] OR "air quality" OR "nitrogen dioxide" [MeSH] OR "sulfur dioxide" [MeSH] OR "carbon monoxide" [MeSH] OR "ozone" [MeSH] OR "particulate matter" [MeSH] OR "nitrogen oxides" [MeSH] OR "PM2.5" OR "PM10" OR "NO2" OR "NOx" OR "O3" OR "SO2" (Title/Abstract) AND "depression" [MeSH] OR “depressive” OR "mood disorder*" [MeSH] OR "mental health" [MeSH] OR “mental disorder” OR "affective disorder*" “mental illness” OR "bipolar disorder*" [MeSH] OR “psychiatric” OR "psychotic" OR “psychosis” OR "schizophrenia" OR "anxiety" OR “PTSD” OR “suicide” OR “self-harm” OR “suicidal” OR “affective” OR “psychological distress” AND NOT (“smoking” OR “smoke”) (Title/abstract). The search was filtered by in the last 10 years, humans, and English language.

PsychInfo: ("air pollution" OR "pollutant*" OR "air quality" OR "nitrogen dioxide" OR "sulfur dioxide" OR "carbon monoxide" OR "ozone" OR "particulate matter" OR "nitrogen oxides" OR "PM2.5" OR "PM10" OR "NO2" OR "NOx" OR "O3" OR "SO2") [Abstract] AND ("depression" OR “depressive” OR "mood disorder*" OR "mental health" OR “mental disorder” OR "affective disorder*" “mental illness” OR "bipolar disorder*" OR “psychiatric” "psychotic" OR “psychosis” OR "schizophrenia" OR "anxiety" OR “stress” OR “PTSD” OR “suicide” OR “self-harm” OR “suicidal” OR “psychological distress” OR “affective”) [Abstract]. NOT (“smoking” OR “smoker”) (Abstract). The search was filtered by in the last 10 years, humans, and English language.

Web of Science: ("air pollution" OR "pollutant*" OR "air quality" OR "nitrogen dioxide" OR "sulfur dioxide" OR "carbon monoxide" OR "ozone" OR "particulate matter" OR "nitrogen oxides" OR "PM2.5" OR "PM10" OR "NO2" OR "NOx" OR "O3" OR "SO2") [Title] AND ("depression" OR “depressive” OR "mood disorder*" OR "mental health" OR “mental disorder” OR "affective disorder*" “mental illness” OR "bipolar disorder*" OR “psychiatric” "psychotic" OR “psychosis” OR "schizophrenia" OR "anxiety" OR “stress” OR “PTSD” OR “suicide” OR “self-harm” OR “suicidal” OR “psychological distress” OR “affective”) [Title]. NOT (“smoking” OR “smoker”) [Title]. The search was filtered by in the last 10 years and English language.

Cinahl: ("air pollution" [MeSH] OR "pollutant*" [MeSH] OR "air quality" OR "nitrogen dioxide" [MeSH] OR "sulfur dioxide" [MeSH] OR "carbon monoxide" [MeSH] OR "ozone" [MeSH] OR "particulate matter" [MeSH] OR "nitrogen oxides" [MeSH] OR "PM2.5" OR "PM10" OR "NO2" OR "NOx" OR "O3" OR "SO2") [Abstract] AND ("depression" [MeSH] OR “depressive” OR "mood disorder*" [MeSH] OR "mental health" [MeSH] OR “mental disorder” OR "affective disorder*" “mental illness” OR "bipolar disorder*" [MeSH] OR “psychiatric” "psychotic" OR “psychosis” OR "schizophrenia" OR "anxiety" OR “stress” OR “PTSD” OR “suicide” OR “self-harm” OR “suicidal” OR “psychological distress” OR “affective”) [Abstract]. NOT (“smoking” OR “smoker”) [Abstract]. The search was filtered by the last 10 years and English language.

2.2.7 Selection Process

Endnote was used to exclude duplicates. Then a manual search for duplicates was done by Ella Christoforou (EC). Independently Cynthia Decourcey (CD) and EC screened the remaining articles title and abstract shown in the table linked here. Any disagreements were resolved by Amy Mizen (AM) which is shown in the table linked here. Full text eligibility was carried out by EC with assistance from AM demonstrated in the table linked here. Due to project time constraints; it was not feasible to do citation searches on 87 articles. Therefore, citation searching was done on ten randomly selected articles from the psychotic experiences, suicide, and anxiety outcome categories. The online website Random Lists was used to randomly select the ten articles from the 87. The articles randomly selected were:

- Lee *et al.,* 2022
- Kim *et al.,* 2018
- Astudillo-García *et al.,* 2019
- Aguglia *et al.,* 2021
- Newbury *et al.,* 2019
- Antonsen *et al.,* 2019
- Brunst *et al.,* 2019
- Diaz *et al.,* 2020
- Yolton *et al.,* 2019
- Zhao *et al.,* 2020

Using google scholar, a citation search was carried out on the ten articles. However, the articles found were limited and either were of poor quality/didn't fit the inclusion criteria.

2.2.8 Data Collection Process

On the articles selected the data extraction process was performed on each article independently by EC. Five random articles were selected for AM to data extract from. A comparison was then made between the two individuals' work. The document which shows these comparisons is linked here. These results were discussed and integrated to quality assess EC's work so the data extraction process could be continued effectively.

2.2.9 Data Items

Data was collected on:

1. Author and publication year
2. Country
3. Study design
4. Study participants- where they are from
5. Characteristics- number, age including mean and range, as well as sex
6. Outcome- mental health or well-being, measurement, when, number, and sex
7. Studied pollutant(s)
8. Exposure- concentration, assessment, short-/long-term/both and resolution
9. Adjustment variables
10. Main results- effect estimates with corresponding 95% confidence intervals (CI)

Some of the data items collected will be explained in more detail to help enable a clear understanding of what data was extracted from the studies.

2.2.9.1 Study Design Types and Terminology

Research study designs are a framework, or the set of methods and procedures used to collect and analyse data on variables specified in a particular research question (Ranganathan & Aggaral, 2018). The terminology used to describe research designs are summarised in **Table 2.4** below.

Table 2.4- Study design terminology.

Term	Definition
Ecologic	Groups of people in different locations.
Backward	Line of enquiry starts with outcome and determines exposure.
Forward	Direction of enquiry moves from exposure to outcome.
Longitudinal	Over time.
Transversal	Observations about exposure and outcome are made at a single point.
Prospective	Involving a period of follow-up after the start of the study
Retrospective	Outcome of interest has already occurred when the study commences. These studies often use medical records or registry data.

There are many different study designs, each with its advantages and limitations. The type of study design used to answer a particular research question is determined by the nature of question, the goal of research, and the availability of resources (Ranganathan & Aggaral, 2018). Although, some of the studies in this review specifically identified the study design however, others were not as clear (Sun *et al.,* 2020). Consequently, some study designs were determined subjectively by EC and concurred by AM. Overall, the study design can affect the validity of its results therefore it is important to understand the different types of designs and their strengths as well as limitations (Ranganathan & Aggaral, 2018). The different types of study designs and their strengths as well as limitations are outlined in **Table 2.5** blow.

Descriptive Studies

- Case study- describes the experience with symptoms, signs, diagnosis, or treatment of a patient.

Analytical Studies

Try to prove a hypothesis and establish an association between an exposure and an outcome. These studies usually have a comparator group.

- Observation (**Table 2.5**)
- Interventional

Table 2.5- Observational study designs of the papers included in the review.

Observational studies	**Research Design**
Cohort	• Direction of enquiry begins with exposure, then proceeds to the outcome (Ranganathan, 2019). • Exploit spatial variations in long-term average concentrations of pollutants (COMEAP, 2020). • Can detect effects such as the increased risk of induction of new disease, or of mortality (COMEAP, 2020). • Strongest among the observational study designs. • Limitations: - Follow-up may not be complete. - Not suitable for rare outcomes. - Unknown confounders other than the exposure affecting the occurrence of the outcome.
Cross-sectional	• Transversal studies- data collected from the study population at a single point in time (Ranganathan, 2019). • Exposure and outcome are determined simultaneously. • Information on prevalence of health conditions and possible associations between risk factors and outcomes. • Not possible to establish a clear cause–benefit relationship.
Case-crossover	• Relatively new analytical epidemiological approach developed to study the effects of transient, short-term exposures on the risk of acute events (Maclure, 1999). • Population have experienced the health outcome of interest. • Each subject serves as his/her own control, so individuals are compared to themselves at different times thus reducing the risk of any residual confounders (age, sex, socioeconomic status) influencing the outcome (Maclure, 1999). • Time-stratified design controls for the day-of-the-week, seasonality, long-term trend, and spatial variation (Wu *et al.,* 2021).

	• Conclusion is based on a comparison of exposure distribution rather than the risk of disease (Jaakkola, 2003).
Time-series	• Examine how routine medical statistics respond to day-to-day variations in pollutant concentrations (Velicer *et al.,* 2010). • Involves single subjects/research units that are measured repeatedly at regular intervals over time (Velicer *et al.,* 2010).
Panel data (time-series cross sectional data)	• Data from many units, over many points in time (Beck, 2001). • Greater capacity for capturing the complexity of human behaviour than a single cross-section or time-series data.

2.2.9.2 Outcome

A mental health or well-being issue defined most often by a diagnosis or questionnaire/scale.

2.2.9.3 Exposure

Air pollution exposure is assessed using methods such as fixed-site monitoring or Land Use Regression (LUR). The concentration is usually measured in $\mu g/m^3$ which means micrograms (one-millionth of a gram) of a pollutant per cubic metre of air. Short-term exposure generally refers to mean exposure over periods of hours, days, or weeks (which is usually measured immediately or only a short time prior to outcome assessment, *i.e.,* at a short lag), often assessed through time-series or case-crossover study designs (Braithwaite *et al.*, 2019). Whereas long-term exposure generally refers to mean exposure over a period of years and, in some studies, of several months, typically assessed through cohort, cross-sectional, or case–control study designs (WHO, 2013; Cai *et al*. 2016).

2.2.9.4 Adjustment Variables

Covariate adjustment is another name for controlling for baseline variables such as sex when estimating exposure effects (Kaufman, 2017). This is often done to improve the precision and power of results (Dolan, 2020).

2.2.9.5 Statistics

The main results column in the data extraction table will provide information on the association between air pollution and mental health. Some of the terminology and the statistical associations used to quantify the associations found in these studies is described in **Table 2.6** below.

Table 2.6- Statistical Terminology.

Terminology	Definition
Statistical test	A mathematical procedure to determine whether a pattern is likely to be due to chance (Dahiru, 2008).
Association	General relationship: when one variable provides information about another (Altman & Krzywinski, 2015).
Correlation	Is more specific: when two variables display an increasing or decreasing trend (Altman & Krzywinski, 2015).
p-value	The probability of obtaining the observed result of a test, assuming the null hypothesis is correct (Dahiru, 2008). The *'p'* stands for probability and measures how likely it is that any observed difference between groups is due to chance (Dahiru, 2008).
Level of significance	$p>0.05$ (5%) means the null hypothesis cannot be rejected (Dahiru, 2008).
Significant	Usually $p<5\%/0.05$ means the result is not due to chance and the null hypothesis can be rejected (Dahiru, 2008).
Odds ratio (OR)	Is equal to **(odds of the event in the exposed group) / (odds of the event in the non-exposed group).** A measure of how strongly an event is associated with exposure (Tenny & Hoffman, 2022). The larger the OR the higher odds that the event will occur with exposure. ORs smaller than one implies the event has fewer odds of happening with the exposure. OR of 1 means there is no association between the exposure and outcome. As odds of an event are always positive, the OR is always positive and ranges from zero to very large.

Relative risk (RR)	Is a ratio of probabilities of the event occurring in all exposed individuals versus the event occurring in all non-exposed individuals (Tenny & Hoffman, 2022). If the RR is greater than 1, then the event is more likely to occur if there was exposure (Tenny & Hoffman, 2022). If the RR is less than 1, then the event is less likely to occur if there was exposure (Tenny & Hoffman, 2022). Like in ORs, the value 1 indicates no difference between the groups.
Excess risk (ER)	Excess rate a particular health effect occurs associated with exposure. Excess risk per unit of exposure divided by the background risk (Lee, 2015).
Relative excess risk (RER)	Comparative effect measure specifically designed to compare the effects of two different exposures (or treatments) (Lee, 2015).
Relative risk increase (RRI)	The increase in rates of bad events, comparing the experimental patients to control patients (Lee, 2015).
Hazard ratio (HR)	The **ratio of (risk of outcome in one group) / (risk of outcome in another group)**, occurring at a given interval of time (Brody, 2016). Hazard ratio of 1 means no association, a hazard ratio greater than 1 suggests an increased risk, and a hazard ratio below 1 suggests a smaller risk (Brody, 2016).
Incidence rate ratio (IRR)	Interpreted like odds ratios (Sedgwick, 2010). Allows comparison of the incident rate between two different groups (Sedgwick, 2010). Greater than 1: incident rate is greater in the exposed compared to unexposed group. Less than 1: incident rate is lower in the exposed compared to unexposed group. Equal to 1: incident rate is equal among those in the exposed and unexposed group.
95% Confidence interval (CI)	A range of values within which it is highly probable (95%) that the true value lies (Sedgwick, 2010; Tenny & Hoffman, 2022).

2.2.10 Quality Assessment

Joanna Briggs Institute (JBI) critical appraisal tool was designed for quality assessment of healthcare practice and outcomes. Therefore, does not facilitate in-depth critical appraisal of air pollution exposure assessment methods. Nevertheless, there does not appear to be a more robust quality assessment tool for a range of study designs. Therefore, JBI tool was used to assess the trustworthiness, relevance, and results of the published papers (Ma *et al.,* 2020). The checklist for cohort, case study, case control and cross-sectional studies was used (Ma *et al.,* 2020). However, because a checklist was not found for case-crossover studies the case-control JBI checklist was used which was the most appropriate. For time-series studies the cohort JBI checklist was used. Studies with panel data were reviewed using the cross-sectional critical appraisal checklist. This was carried out by EC on all papers. As a quality assurance measure AM quality assessed five articles. The studies which were quality assessed by both authors are linked here. These results were discussed and integrated to help assess the quality of the other studies. The data extraction table included a column on comments/limitations including consideration from the JBI checklist and the quality of the studies. Although, there are few widely acknowledged quality standards for research practice, and few definitions of what constitutes good research (Mårtensson *et al.,* 2016; Anjana & Choudhuri, 2018). Therefore, a criterion for low, moderate, and high-quality studies was developed to aid quality assessment which is shown in **Table 2.7** below.

Table 2.7- Characteristics used to define low, moderate, and high-quality studies.

Quality	Characteristics
Low	• Unreliable mental health assessment (Hopwood *et al.,* 2018) • Lack of detail on how mental health and air pollution were defined. • Low number of participants can undermine the validity of the results (Faber & Fonseca, 2014). • No statistical testing. • Limited methodological detail. • Not peer reviewed (Anjana & Choudhuri, 2018) • Cross-sectional studies of long-term exposure using an exposure period overlapping with or after outcome assessment (Braithwaite *et al.,* 2019)
Moderate	• Some consideration of confounding variables such as meterological variables but no other important risk factors *e.g.,* deprivation (Braithwaite *et al.,* 2019). • Lacks a reliable tool to assess mental health *e.g.,* self-reported measures without quantifiable results (Althubaiti, 2016) • Cross-sectional studies of long-term exposure corresponding to a period prior to the outcome assessment period (Braithwaite *et al.,* 2019) • Air pollution assessment using only monitoring stations as this may not accurately measure everyday exposure (Briggs *et al.,* 1997; Briggs, 2005). • Time stratified case cross-over design controls for time (day, month, and year), temperature and short-term time invariant potential confounders (age, sex, socioeconomic status) (Peters *et al.,* 2006).
High	• Data from multiple healthcare settings which is more representative. • Clear how mental health was assessed with a reliable clinical tool *e.g.,* GAD-2 scale (Hopwood *et al.,* 2018) • Various confounding variables adjusted for *e.g.,* socioeconomic factors, physical activity, smoking status, and area-level deprivation which are considered important (Braithwaite *et al.,* 2019; Dolan, 2020). • Larger number of participants • Detailed description of participant demographic variables

	• Pollution measured at multiple locations which could more accurately represent everyday exposure. • Air pollution exposure assessment tools with finer spatial and temporal resolution to characterize individual exposure, such as LUR models (Briggs *et al.,* 1997; Briggs, 2005). • Multiple pollutants considered (COMEAP, 2020) • Time stratified case cross-over design which controls for various factors as described in the moderate quality section (Peters *et al.,* 2006).

2.2.11 Data Analysis

Once the final number of articles were selected for the review, the total number of articles were categorized by study design, location, exposure length, how exposure was measured, the mental health outcome and how it was measured (**Figure 2.1** on page 59). The data extraction tables were organised by mental health outcome. This was also done within the review in which associations described in the studies were organised according to the mental health outcome in the syntheses.

2.3 Results

2.3.1 Literature retrieval and study characteristics

Out of 2,224 publications identified, 2,010 were non-duplicates and 222 were eligible for inclusion after the screening of the title and abstract. After full-text eligibility 153 articles were left. Due to the high number of articles to review and concerns around the feasibility of completing data extraction the exclusion criteria were updated to include pregnancy (14 articles), articles published in 2011 (4 articles) and articles with depression or depressive symptoms as the only outcome (48 articles). Of the 153 publications, 87 met the inclusion criteria and therefore were included in the review (**Figure 2.2**). This process is shown in **Figure 2.2** and reasons for the exclusion of full-text articles is explained. The main characteristics of the included studies are described in terms of the study design, the country the study was conducted in, exposure length, how exposure was derived, mental health outcomes and how these outcomes were defined. The quality of studies was also assessed by the JBI tool depending on their study design.

Out of the 87 included studies their number and design were: 15 case-crossover, 23 cohort, 22 cross-sectional, 24 time-series and four panel studies. The critical appraisal table linked here shows the quality of the studies based on their study design.

The majority, 42 studies were conducted in Asia, 26 in Europe, 17 in North America and two studies were conducted in multiple countries across multiple continents.

Regarding exposure to air pollution, 50 studies evaluated short-term effects (<6 months), 34 studies evaluated long-term effects (≥6 months) and three explored both short- and long-term effects. Exposure to air pollutants was derived from monitoring/measuring stations or sites in 50 of the studies, while it was estimated through Land Use Regression (LUR) models in six studies and chemical transport or spatiotemporal models in nine of the studies. Eight other types of modelling were also used: combined modelling in one study, universal kriging in one study, KCLurban in three studies, integrated air pollution dispersion system in one, and Community Multiscale Air Quality (CMQ) in two studies. Portable devices were used in one study, online databases in seven and multiple measures in six studies.

The mental health disorders and well-being categories were defined as psychotic disorders which consisted of 13 studies, anxiety included 14 studies, one study had an outcome of mania, mortality related to mental illness/well-being consisted of four studies and 14 studies were suicide related. In terms of self-reported mental health and well-being, three had an outcome of overall mental health/well-being, eight had an outcome of psychological stress or distress and ten had an outcome of multiple measures of well-being/mental health. The outcome contact with mental health professionals for multiple psychiatric disorders contained 18 studies. Forty-eight studies had an outcome of only depression or depressive symptoms, and these were excluded. The data extraction tables are linked according to the mental health outcome.

Mental health outcomes were defined using ICD-10 (mainly) and versions 8/9 in 33 studies, scale/questionnaires in 28 studies, and hospital visits in five studies. Additionally, in four studies interviews based on DSM-IV plus a scale were used, ICD9-CM in three studies, ICD-10 plus a scale in two studies and two studies also used interviews.

Suicide mortality statistics were collected from four different databases in four different studies: National Institute of Statistics and Geography, medical examiner, Polish Police Headquarters and Chief Inspectorate for Environmental Protection, UK's Department of Health. The mental health outcomes in the 'other' category consisted of different outcomes for each of the six studies: ICD-10 plus national patient register, emergency ambulance dispatches, interview plus questionaire, scale plus anxiety prevalence, International Classification of Primary Care (ICPC), and ICD9-CM plus ICD-10.

The study characteristic described above are shown in **Figure 2.1** below.

2.3.1.1 Summary of Study Characteristics

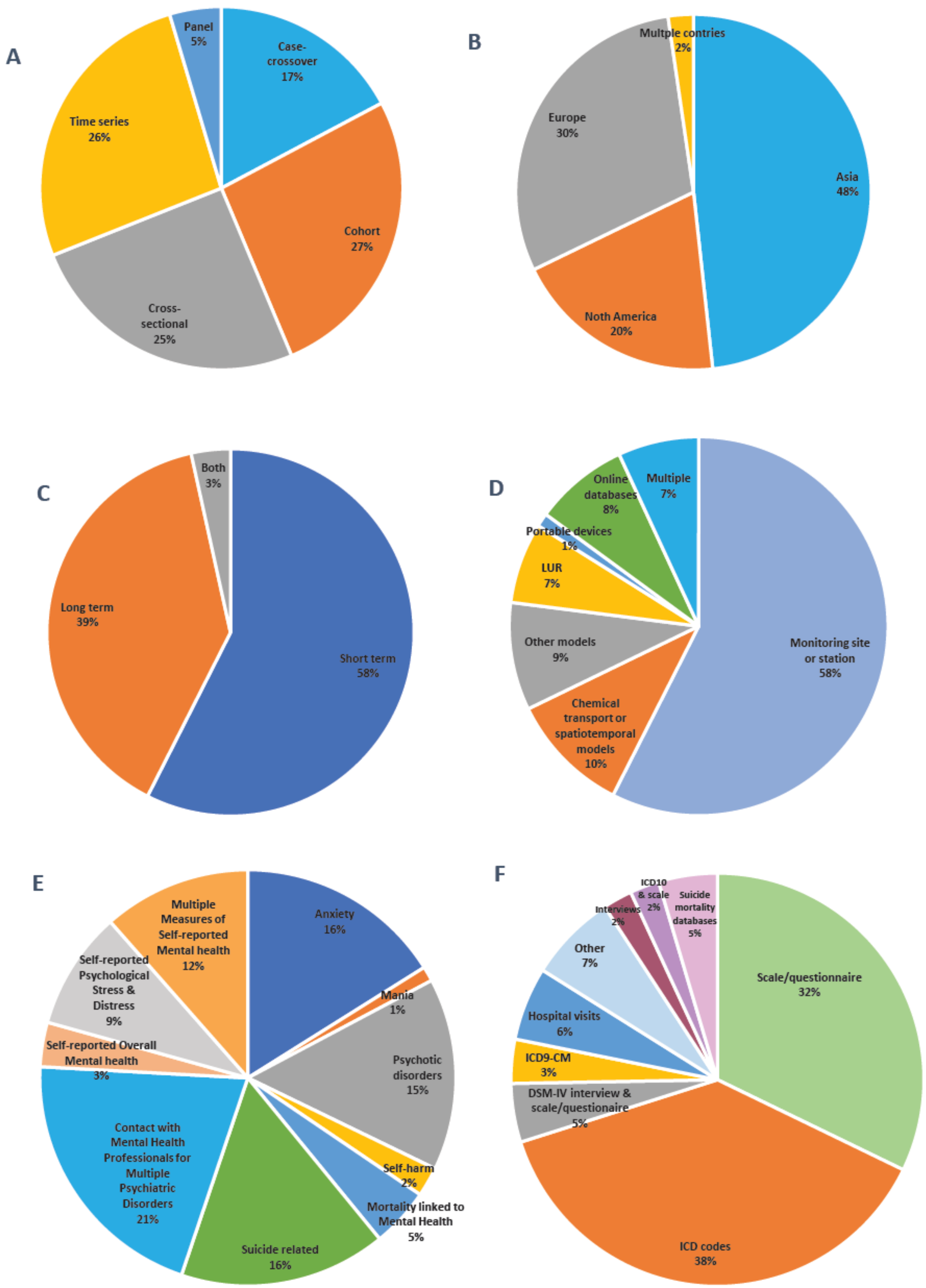

Figure 2.1- Study characteristics. The first line represents **(A)** study design, and **(B)** location studies were conducted in. The second line describes **(C)** exposure length and **(D)** how it was defined in the studies. The third line represents the **(E)** mental health outcomes in terms of the type and **(F)** how they were defined.

2.3.1.2 PRISMA Flow Diagram

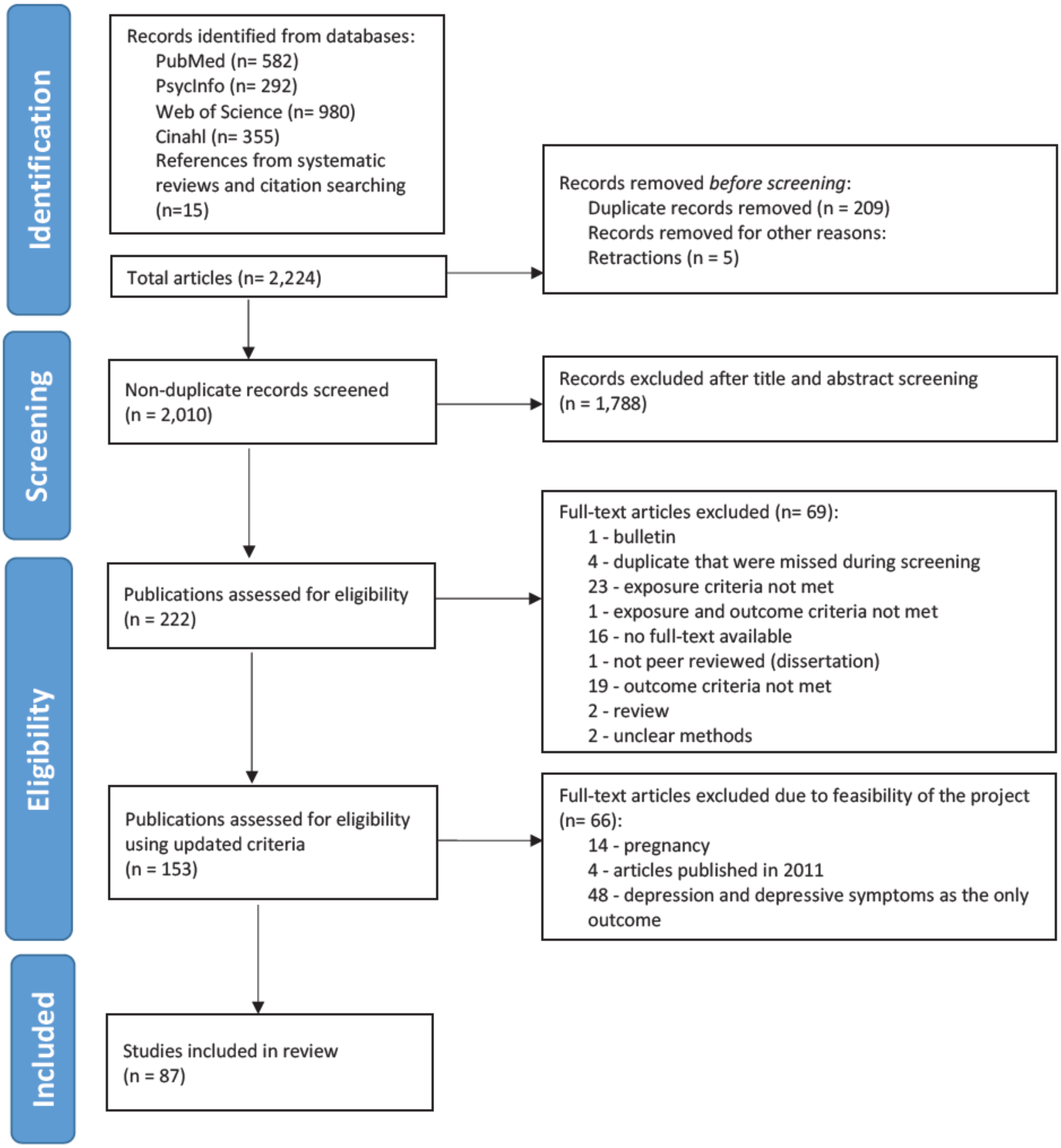

Figure 2.2 - PRISMA flow diagram. This shows the study selection procedure (Page *et al.*, 2021).

2.3.2 Psychotic Disorders

In the outcome psychotic disorders 13 studies were identified. The data extraction table for psychotic disorders is linked here. The effects of pollutants on psychosis or psychotic experiences in three studies and schizophrenia in ten studies were investigated. In one study schizophrenia was diagnosed using DSM-IV (Gao *et al.,* 2021). In another psychotic experiences were defined using an interview involving six items on unusual feelings and thoughts including seven items on hallucinations/delusions with clinical verification (Newbury *et al.,* 2019). These items drew on item pools since formalised in prodromal psychosis screening instruments including the Prevention through Risk Identification, Management and Education (PRIME)-screen and the Structured Interview for Psychosis-Risk Syndromes (SIPS) (Newbury *et al.,* 2019). In the ten other studies psychosis and schizophrenia were diagnosed using ICD-10. The pollutants investigated were:

- Multiple pollutants in different combinations ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, CO, NO_x) in six studies (Tong *et al.,* 2016; Duan *et al.,* 2018; Lian *et al.,* 2019; Newbury *et al.,* 2019; Antonsen *et al.,* 2020; Lee *et al.,* 202).
- $PM_{2.5}$ and PM_{10} in three studies (Bai *et al.,* 2020; Ji *et al.,* 2021; Wei *et al.,* 2021),
- $PM_{2.5}$ only in two studies (Eguchi *et al.,* 2018; Gao *et al.,* 2021)
- NO_2 only in two studies (Bai *et al.,* 2019; Horsdal *et al.,* 2019)

2.3.2.1 Psychotic Experiences

Three studies investigated psychotic experiences and the effects of long-term (Newbury *et al.,* 2019) and short-term exposure (Tong *et al.,* 2016; Lee *et al.,* 2022).

In the cohort study by Newbury and colleagues, 18-year-old participants in the UK were interviewed about their previous psychotic experiences from the age of 12 to the current day. This was linked to their previous annual exposure to multiple pollutants (NO_2, NO_x, $PM_{2.5}$, PM_{10}) the year before they were interviewed (Newbury *et al.,* 2019). This study found adolescents exposed to the highest annual levels of air pollution (26.0 µg/m^3 for NO_2, 33.0 µg/m^3 for NO_x, 12.4 µg/m^3 for $PM_{2.5}$, and 17.6 µg/m^3 for PM_{10}) reported higher rates of psychotic experiences than adolescents exposed to lower levels. Positive associations were found for PM_{10} (OR 1.27 [95% CI 0.98-1.65]) (Newbury *et al.,* 2019). However, significant positive associations were demonstrated for NO_2, NO_x, and $PM_{2.5}$ after adjustment for all covariates respectively (OR 1.71 [1.28-2.28] $p<0.001$, OR 1.72 [1.30-2.29] $p<0.001$, and OR 1.45 [1.11-1.90] $p<0.01$) (Newbury *et al.,* 2019). Psychotic experiences were significantly more common in the most urban vs rural neighbourhoods at age 18 (OR, 1.93; 95% CI, 1.35-2.75) (Newbury *et al.,* 2019). Together NO_2 and NO_x statistically explained 60% of the association between urbanicity and adolescent psychotic experiences (Newbury *et al.,* 2019). This study was high-quality as family socioeconomic status and clinical history, maternal and childhood psychotic symptoms were adjusted for. The consideration of poor parental mental health is important as it has been shown to cause greater distress through adulthood than in non-exposed counterparts (Kamis *et al.,* 2020). There was also adjustment for adolescent smoking and substance dependence. Moreover, air pollution was measured at participants' residence plus two commonly visited locations which could provide a more accurate air pollution exposure estimate.

Lee *et al*. (2022) investigated the impact of previous week exposure to increasing concentrations of air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, CO) on the risk of emergency department visits for psychosis in Korea. Visits to the emergency department were noted as positive and significant following exposure to interquartile range increases in:

- $PM_{2.5}$ (per 14.93 μg/m^3; OR = 1.028; 95% CI: 1.006, 1.049),
- PM_{10} (per 28.41 μg/m^3; OR = 1.022; 95% CI: 1.003, 1.040),
- SO_2 (per 2.13 ppb; OR = 1.030; 95% CI: 1.003, 1.058) all at lag 6.
- NO_2 (per 17.69 ppb; OR = 1.037; 95% CI: 1.007, 1.068) at lag 7.

The associations found for O_3 (per 22.84 ppb; 0.981 95% CI: 0.948, 1.016) and CO (per 2.87 ppm; 1.019 95% CI 0.995, 1.044) were non-significant (Lee *et al.,* 2022). In addition, these associations were higher among male patients and in the cold season. Lee and colleague's found short-term exposure to the highest quartile generally showed a higher risk of psychosis compared to the lower quartile for:

- $PM_{2.5}$ (>30.22 μg/m^3): OR = 1.046 (0.984, 1.112); Ptrend = 0.097,
- NO_2 (>42.85 ppb): OR = 1.129 (1.058, 1.205); Ptrend = 0.001,
- SO_2 (>6.07 ppb): OR = 1.054 (0.976, 1.137); Ptrend = 0.090.

Similarly, a time-series study conducted in a Chinese city found an increase of 10 μg/m^3 in 2-day average concentration of PM_{10}, SO_2, and NO_2 corresponded to 0.06% (0.02, 0.10), 0.10% (0.01, 0.19) and 0.17% (0.07, 0.26) increase in daily psychosis hospital admissions respectively (Tong *et al.,* 2016). These associations were significant for PM_{10} and SO_2 over the entire period and only for NO_2 in the cool season.

The study by Lee and colleagues had large number of participants, investigated multiple pollutants, and psychotic experiences were defined by clinician diagnoses. Moreover, the study design controlled for time and short-term time invariant confounders such as sex, age, and deprivation as well as meteorological variables (temperature, humidity, pressure, holidays, sunlight hours and rainfall). However, city level pollutant concentrations may not be accurate of individual exposure. Therefore, the study was described as moderate to high quality. Whereas Tong and colleagues only adjusted for time and meterological variables (day of the week, calendar time, temperature, humidity). In addition, the study lacked descriptive statistics (sex and age) and the methodology as well as results were unclear. Although, participants were diagnosed with ICD-10, multiple pollutants were measured, and the sample was large (1430). Therefore, the study was classified as low to moderate.

2.3.2.2 Schizophrenia Diagnosis

In terms of the outcomes investigated, six studies had an outcome of schizophrenia hospital admissions, three had an outcome of schizophrenia relapse or re-admissions and one had an outcome of schizophrenia severity. The effects of various pollutants on these outcomes are explained below.

2.3.2.2.1 Hospital Admissions

Overall, six studies investigated schizophrenia hospital admissions. Four were time-series studies conducted in Chinese cities, which investigated short-term exposure (up to 12 days) (Bai *et al.,* 2019; Bai *et al.,* 2020; Duan *et al.,* 2018; Liang *et al.,* 2019). Apart from Bai *et al*. (2020) which focused on PM the other studies explored multiple pollutants.

Positive significant associations were shown between $PM_{2.5}$ on schizophrenia hospital admissions (Bai *et al.,* 2020). Longer exposure and higher concentrations of $PM_{2.5}$ increased hospital admissions. The risk effect generally appeared on the second or third day after exposure to the $PM_{2.5}$ wave, and the pronounced effect mostly presented at lag 6 (Bai *et al.,* 2020). The $PM_{2.5}$ wave, defined as ≥2 consecutive days with concentration of ≥90th (217 μg/m^3), ≥92.5th, ≥95th and ≥97.5th (306 μg/m^3) percentile, was associated with 4.8% (2.0%-7.6%), 4.9% (1.9%-7.9%), 5.5% (2.0%-9.2%), and 7.6% (2.9%-12.6%) increase in hospital admissions for schizophrenia at lag 6 (Bai *et al.,* 2020). The risk increased further at all concentrations when the $PM_{2.5}$ wave was defined as ≥3 consecutive days. For example, at ≥97.5th percentile the RR was 12.0% (5.3%-19.1%) increase in hospital admissions at lag 6 (Bai *et al.,* 2020). Similarly, overall, a 10 μg/m^3 raise of PM_{10}, SO_2, and NO_2 on the same day corresponded to increases in daily schizophrenia outpatient visits 0.289% (95% CI: 0.118%, 0.460%), 1.374% (95% CI: 0.723%, 2.025%), and 1.881% (95% CI: 0.957%, 2.805%), respectively (Liang *et al.,* 2019). Significant associations were observed in all cumulative exposures (lag 01 to lag 03). Co-exposure caused associations to be attenuated substantially and become less statistically significant. Higher levels of PM_{10} and NO_2 were associated with rising risk for schizophrenia visits apart from concentrations over 700 μg/m^3 for PM_{10} and 120 μg/m^3 for NO_2 (Liang *et al.,* 2019). Another study also found a significant positive association to schizophrenia emergency admissions for these pollutants

(NO_2: lag 0–4 RR, 1.84 [95% CI: 1.49–2.27], PM_{10}: lag 0–3 RR, 1.97 [95%CI: 1.57–2.36], SO_2: lag 0–10 RR, 2.93 [95%CI: 2.10–4.10]) (Duan *et al.,* 2018). Significant positive associations between increases in NO_2 at the 75th and 95th percentile and schizophrenia hospital admissions at lag 0, lag 1 and lag 01 (current and previous day) (Bai *et al.,* 2019). The RR per IQR increase in NO_2 at the lag 01 was 1.13 (95% CI 1.05-1.22) when adjusted for CO and PM_{10} (Bai *et al.,* 2019).

It was found that individuals aged 20–59, particularly those <40 were at significantly higher-risk than at other ages (Duan *et al.,* 2018; Bai *et al.,* 2019). However, another study found no significantly statistical difference in schizophrenia risk between patients aged <45 and ≥45 (Bai *et al.,* 2020). Male patients showed a greater risk of schizophrenia onset (Duan *et al.,* 2018). In contrast, a stronger relationship between $PM_{2.5}$ wave and hospital admissions were observed in females than males (Bai *et al.,* 2020). However, Liang *et al.* (2019) demonstrated associations appeared to be stronger, although not statistically significant, in females and those aged >40. Contrastingly, Bai *et al*. (2019) found the RR for men [1.10 (95% CI 1.00 to 1.20)] and women [1.11 (95% CI 1.01 to 1.22)] were similar at lag 01.

These studies were considered moderate quality due to only adjusting for meteorological variables (temperature, sunlight, and humidity). Therefore, there was no consideration of psychological factors (*e.g.,* life events, compliance to treatment, and poor social support) and the effect of other clinical variables. Two of the studies also only used data from a single hospital (Bai *et al.,* 2019, Bai *et al.,* 2020). However, these studies did have large cohorts and the mental health outcome was diagnosed by a clinician.

Two cohort studies conducted in Denmark investigated childhood exposure (from birth till age 10) and risk of a schizophrenia diagnosis after an individual's 10th birthday (Antonsen *et al.,* 2020; Horsdal *et al.,* 2019). Significant positive associations were found per 10 μg/m^3 increase in NO_2 and NO_x respectively and incidence rate ratios (IRR) for schizophrenia risk by age 37, 1.29 (95% CI 1·21–1·39) and 1.06 (95% CI: 1.02, 1.10) (Antonsen *et al.,* 2020). A similar value was found for NO_2 adjusted hazard ratio (AHR) 1.23 (95% CI: 1.15, 1.32) in the Horsdal *et al.* (2019) study. Increasing concentrations of NO_2 were found to increase the risk of schizophrenia diagnoses (Antonsen *et al.,* 2020; Horsdal *et al.,* 2019). People exposed to daily mean concentrations of more than 26.5 μg/m^3 NO_2 had a 1.62 (95% CI: 1.41, 1.87) times increased risk compared with people exposed to mean daily concentrations of less than 14.5 μg/m^3 (Antonsen *et al.,* 2020). Individuals exposed to daily NO_2 levels of 25 μg/m^3 or higher during childhood had an increased risk compared with individuals exposed to daily levels less than 10 μg/m^3 (AHR, 1.62; 95% CI, 1.25-2.12) (Horsdal *et al.,* 2019). Men were found to be at increased risk at higher concentrations compared to women (Antonsen *et al.,* 2020). The risk of developing schizophrenia by age 37 when exposed to daily mean concentrations of more than 26.5 μg/m^3 of NO_2 between birth and 10 years was 1.45% (95% CI 1.30–1.62%) for men and 1.03% (95% CI 0.90–1.17) for women (Antonsen *et al.,* 2020). Whereas when exposed to concentrations less than 14.5 μg/m^3 the risk was 0.80% (95% CI 0.69–0.92%) for men and 0.67% (0.57–0.79) for women (Antonsen *et al.,* 2020). In contrast, the links with $PM_{2.5}$ and PM_{10} were less clear and consistent when concentrations increased. There was little evidence of associations after adjustments for covariates [per 1 μg/m^3 increase of $PM_{2.5}$ IRR 1.02 (95% CI 0.98-1.06) and PM_{10} IRR 1.04 (95% CI 1.0-1.08)] (Antonsen *et al.,* 2020). These were considered high quality studies as parental history of psychiatric disorders, parental socioeconomic position, urbanisation level and demographic variables were adjusted for. In addition to having large cohorts, high exposure resolution and a diverse rural/urban setting.

2.3.2.2.2 Relapse and re-admissions

Three studies investigated relapse and short-term exposure to PM in China (Gao *et al.,* 2021; Ji *et al.,* 2021; Wei *et al.,* 2021). Relapse is a deterioration in someone's state of health after a temporary improvement. Similarly, re-admissions are when an individual is re-admitted to hospital for treatment.

Two studies both used the Early Signs Scale (ESS) which self-assesses the risk of relapse (Gao *et al.,* 2021; Wei *et al.,* 2021). Both studies found that the ESS score increased per 10 μg/m^3 increase in $PM_{2.5}$, the greatest effect was over the last 0-23h (lag0). This was when total ESS score increased by 1.504 (OR 4.50, 95% CI: 2.849–7.106, $P < 0.001$) (Gao *et al.,* 2021) and by 4.112 points (95% CI: 3.174- 5.050, $p<0.001$) (Wei *et al.,* 2021). For each 10 μg/m^3 increase in PM_{10}, the risk of relapse score increased by 2.634 (95%CI: 2.022, 3.245, $p<0.001$) (Wei *et al.,* 2021). Another study found statistically significant associations between short-term exposure to $PM_{2.5}$ as well as PM_{10} and hospital re-admissions in China at varying exposure times (Ji *et al.,* 2021). Statistically significant single lag associations occurred from lag 1 to 4 for $PM_{2.5}$ and lag 2 to 4 for PM_{10}. The strongest single-day effects all occurred on lag3, and the corresponding RRs were 1.07 (95% CI: 1.02–1.11) per 53 μg/m^3 increase in PM_{10}, and 1.05 (95% CI: 1.01–1.09) per 33 μg/m^3 increase in $PM_{2.5}$ (Ji *et al.,* 2021). A significant association for extended exposure varied by pollutant; from lag03 to lag06, with the maximum RR at lag06 (RR 1.25, 95% CI 1.05–1.49) for $PM_{2.5}$ and from lag04 to lag06, with the maximum RR at lag05 (RR 1.23, 95% CI 1.04–1.46). Despite Gao *et al*. (2021) finding that sex did not make a difference, Ji *et al*. (2021) found males were more sensitive to PM than females. Wei *et al*. (2021) only used male participants.

All these studies were defined as moderate quality (Gao *et al.,* 2021; Ji *et al.,* 2021; Wei *et al.,* 2021). Ji and colleagues adjusted for time (long-term trend, day of the week, public holidays) and meterological (humidity, temperature) variables. Although, some demographic (age) and health (BMI) variables were adjusted for, both studies had a short study period (11 and 2 months) and small sample size (58 and 24) (Gao *et al.,* 2021; Wei *et al.,* 2021).

2.3.2.2.3 Severity

One Japanese study explored the relationship between 0–7 days of $PM_{2.5}$ exposure and schizophrenia severity using the Brief Psychiatric rating Scale (BPRS) (Eguchi *et al.,* 2018). The odds ratio (OR) for a BPRS score ≥ 50 (markedly ill) at admission was 1.05 (95% CI 1.00–1.10) in the adjusted model (Eguchi *et al.,* 2018). Although, the effects of $PM_{2.5}$ concentration were only significant at lag2 (Eguchi *et al.,* 2018). For those aged ≥65 years, a significant association between $PM_{2.5}$ (0-7 days) and BPRS scores ≥ 50 resulted in a high OR 1.19 (95% CI 1.04–1.38) at lag6 compared to those aged 20–64 (Eguchi *et al.,* 2018). This was a large high-quality study which considered co-exposure (NO_2, SO_2, O_x, & CO), multiple meteorological, demographic, time, and socioeconomic variables.

The information in this section is summarised in **Tables 2.8** and **2.9** below.

2.3.2.2.4 Summary of Psychotic Disorders and Pollution Associations

All 13 studies found a significant association or increased risk from short- and long-term exposure to different pollutants and psychotic disorders. The associations are detailed in the **Table 2.8** below.

Table 2.8- Summary of the associations found between various pollutants and psychotic disorders.

Pollutant exposure and source	The Association of Pollutants with Psychotic disorders	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Significant positive**:			A significant positive association was found for seven of the studies and one found no association. Therefore, $PM_{2.5}$ could be a risk factor for psychotic disorders.
	Schizophrenia severity	(Eguchi *et al.,* 2018)	Aged >65 vulnerable group.	
	Schizophrenia relapse short-term exposure in Chinese cities.	(Gao *et al.,* 2021)	Score increased by 1.504 points.	
		(Ji *et al.,* 2021)	Low RR 1.05 per 33 μg/m³ increase.	
		(Wei *et al.,* 2021)	Score increased by 4.112 points.	
	Schizophrenia hospitalisation	(Bai *et al.,* 2020)	High concentration (217-306 μg/m³).	
	Psychotic experiences	(Newbury *et al.,* 2019)	OR 1.45 in adolescents which was not affected by covariates.	
		(Lee *et al.,* 2022)	OR = 1.028, dose response relationship	
	No association to schizophrenia hospitalisation	(Antonsen *et al.,* 2020)	IRR 1.02 (95% CI 0.98-1.06) per 1 μg/m³	
PM_{10}	**Significant positive:**			PM_{10} could be a risk factor as most of the

	Schizophrenia hospitalisation	(Liang *et al.,* 2019)	0.29% increase. Inclusion of SO_2 & NO_2 significance was lost.	studies found a positive association apart from one. Although, these associations were reduced compared to other pollutants.
		(Duan *et al.,* 2018)	Lag 0–3, RR 1.97.	
	Schizophrenia relapse	(Ji *et al.,* 2021)	Low RR 1.07 per 53 μg/m^3 increase	
		(Wei *et al.,* 2021)	Score increased by 2.634.	
	Psychotic experiences	(Lee *et al.,* 2022)	OR = 1.022.	
		(Tong *et al.,* 2016)	Smallest percentage change (0.06%).	
	Positive to psychotic experiences	(Newbury *et al.,* 2019)	OR=1.27. Significant for NO_2, NO_x & $PM_{2.5}$ in adolescents.	
	No association to schizophrenia hospitalisation	(Antonsen *et al.,* 2020)	1.04 (95% CI 1.0-1.08) per 1 μg/m^3	
NO_2	**Significant positive**:			NO_2 could be a major risk factor for individuals with psychotic disorders. Since, all eight studies found a significant positive association with various negative effects on psychotic disorders.
	Psychotic experiences	(Newbury *et al.,* 2019)	NO_2 OR 1.71 & NO_x OR 1.72 in adolescents.	
		(Tong *et al.,* 2016)	Highest percentage change (0.17%). Significant only in cool season.	
		(Lee *et al.,* 2022)	OR = 1.037, dose-response relationship.	
	Schizophrenia hospitalisation	(Duan *et al.,* 2018)	Lag 0–4 RR 1.84 Males at high risk.	

		(Bai *et al.,* 2019)	Not effected by co-exposure. Sex & age effects by not significant.	
		(Horsdal *et al.,* 2019)	AHR 1.23 Dose response relationship.	
		(Liang *et al.,* 2019)	Highest percentage increase (1.88%).	
		(Antonsen *et al.,* 2020)	NO_2 IRR 1.29 & NO_x IRR 1.06. Dose response relationship.	
SO_2	**Significant positive**:			Could be a potential risk factor however more research evidence is needed.
	Psychotic experiences	(Lee *et al.,* 2022)	OR = 1.030, dose-response relationship	
		(Tong *et al.,* 2016)	Smaller than NO_2 percentage change (0.10%).	
	Schizophrenia hospitalisation	(Liang *et al.,* 2019)	1.37% increase.	
		(Duan *et al.,* 2018)	Lag 0–10 RR 2.93; longest exposure & largest coefficient.	
O_3	**Negative association** to psychosis	(Lee *et al.,* 2022)	0.981 (95% CI: 0.948, 1.016). Non-significant.	Lacks research evidence so further clarity is needed.
CO	**Positive association** to psychosis	Lee *et al.,* 2022)	1.019 (95% CI 0.995, 1.044). Non-significant.	More research evidence needed.

- Individuals with psychotic disorders could be most at-risk from NO_2 exposure.

The quality assigned to the studies in this section is summarised in the **Table 2.9** below.

Table 2.9- Study quality described in the table below.

Quality	**Study Citation**
Low to moderate	(Tong *et al.,* 2016)
Moderate	(Duan *et al.,* 2018; Bai *et al.,* 2019; Liang *et al.,* 2019; Bai *et al.,* 2020; Gao *et al.,* 2021; Ji *et al.,* 2021; Wei *et al.,* 2021)
Moderate to high	(Lee *et al.,* 2022)
High	(Eguchi *et al.,* 2018; Horsdal *et al.,* 2019; Newbury *et al.,* 2019 Antonsen *et al.,* 2020)

2.3.3 Suicide Related

In total 14 studies had an outcome related to suicide. The data extraction table for suicide related disorders is linked here. In terms of the specific outcome, one study investigated suicide attempt, one investigated ideation and 12 studies investigated mortality. A suicide attempt was defined by emergency department visits (Aguglia *et al.,* 2021). The PHQ-9 was used to define suicide ideation (Luo *et al.,* 2020). Mortality was defined in eight studies by an ICD-10 diagnosis (Casas *et al.,* 2017; Fernández-Niño *et al.,* 2018; Kim *et al.,* 2015; Kim *et al.,* 2018; Lee *et al.,* 2018; Lin *et al.,* 2016; Min *et al.,* 2018; Ng *et al.,* 2016). In four studies the only information given about the outcome was where the information was taken from; the National Institute of Statistics and Geography (Astudillo-García *et al.,* 2019), medical examiner (Bakian *et al.,* 2015), Polish Police Headquarters and Chief Inspectorate for Environmental Protection (Gładka *et al.,* 2021) and the UK's Department of Health (Sun *et al.,* 2020). In terms of the pollutant studied:

- 11 investigated multiple pollutants (PM_{10}, $PM_{2.5}$, CO, NO_2, SO_2, O_3, suspended particulate matter [SPM]),
- One focused on $PM_{2.5}$ (Sun *et al.,* 2020),
- One on PM_{10} and $PM_{2.5}$ (Gładka *et al.,* 2021)
- One on PM_{10} and O_3 (Casas *et al.,* 2017)

2.3.3.1 Suicide Attempt

One study explored suicide attempt and monthly exposure to multiple pollutants (PM_{10}, $PM_{2.5}$, CO, NO_2) in a time-series study (Aguglia *et al.,* 2021). A positive correlation (32%) was found between $PM_{2.5}$ and high-lethality suicide attempt in an Italian hospital, with a zero-time lag (Aguglia *et al.,* 2021). Therefore, an increase in $PM_{2.5}$ corresponds with an increase in suicide attempts albeit with a relatively low degree of correlation (Aguglia *et al.,* 2021). High-lethality suicide attempt was defined as a suicide attempt that warranted hospitalization for at least 24 hours and treatment in a specialized unit or extensive medical treatment. This study was described as moderate quality, because it was a small study (67 suicide attempts), only meterological variables (*e.g.,* temperature, precipitation, wind speed, relative humidity) were adjusted for, and data was from one hospital.

2.3.3.2 Suicide Ideation

The Henan Rural cohort study was conducted in multiple cities in China and explored the association between multiple air pollutants (PM_1, $PM_{2.5}$, PM_{10}, NO_2) and suicide ideation (Luo *et al.,* 2020). Positive significant associations were found between suicide ideation and 1 μg/m^3 increase in PM_1, $PM_{2.5}$, PM_{10} and NO_2 concentration with ORs (95% CIs) 1.08 (1.01, 1.15), 1.10 (1.02, 1.19), 1.05 (1.01, 1.09) and

1.12 (1.04, 1.21), respectively. Those exposed to the highest quartile of PM_1, $PM_{2.5}$, PM_{10} or NO_2 had a 1.36-fold (95% CI: 1.08, 1.72), 1.69-fold (95% CI: 1.05, 2.72), 1.49-fold (95% CI: 1.09, 2.05) or 1.71-fold (95%CI: 1.15, 2.85) increase in suicide risk, compared to those with the lowest corresponding concentration (Luo *et al.,* 2020). The risk of suicide appeared to significantly increase with the air pollutant quartiles (PM_1: Ptrend = 0.002, $PM_{2.5}$: Ptrend = 0.003, PM_{10}: Ptrend = 0.010, NO_2: Ptrend = 0.010). The susceptible subgroups found had higher ORs with each 1 μg/m^3 increase in pollutants: males ($PM_{2.5}$: 1.16 vs. 1.06, PM_{10}: 1.10 vs. 1.03), highly educated (1.15 vs. 1.03 for $PM_{2.5}$, 1.19 vs. 1.06 for NO_2) and aged 36–64 years (1.10 vs. 0.93 for PM_1, 1.14 vs. 0.92 for PM2.5, 1.07 vs. 0.95 for PM_{10}).

This was classified as a high-quality study because population characteristics were described, suicide ideation was measured using a clinical tool (PHQ-9), and there was adjustment for various health behaviours (*e.g.,* physical activity, body mass index [BMI], smoking status, and presence of a chronic disease) and demographic variables (*e.g.,* age, gender, educational level, and average monthly income).

2.3.3.3 Suicide Mortality

Of the 12 studies with an outcome of mortality, three investigated annual exposure to $PM_{2.5}$ (Sun *et al.,* 2020), $PM_{2.5}$ and PM_{10} (Gładka *et al.,* 2021) as well as PM_{10}, SO_2, NO_2 (Min *et al.,* 2018). Short-term exposure to various pollutants ($PM_{2.5}$, PM_{10}, O_3, NO_2, SO_2, CO) up to seven days (Bakian *et al.,* 2015; Lin *et al.,* 2016; Ng *et al.,* 2016; Casas *et al.,* 2017; Fernández-Niño *et al.,* 2018; Kim *et al.,* 2018; Lee *et al.,* 2018; Astudillo-García *et al.,* 2019) and six weeks (Kim *et al.,* 2015) prior to a suicide event.

A cross-sectional study showed suicides rates in London were positively associated with annual $PM_{2.5}$ exposure (Pearson's R value= 0.577) (Sun *et al.,* 2020). Furthermore, in the spatial regression models $PM_{2.5}$ level had a statistically significant association with suicide rate (2.102 and 1.982, p=0.001) (Sun *et al.,* 2020). Similarly, Gładka and colleagues found a positive association for $PM_{2.5}$ including PM_{10} in Poland. A unit increase in $PM_{2.5}$ and PM_{10} was correlated with a 0.549 and 0.54 increase in suicide rate in the monovalent regression analysis (p = 0.001) (Gładka *et al.,* 2021). Significant ($p < 0.001$) relationship was found between $PM_{2.5/10}$ exposure and suicide among women (R = 0.987) (Gładka *et al.,* 2021). A prospective national cohort study in South Korea found, increases in 7.5 μg/m^3 of PM_{10}, 11.8 ppb of NO_2, and 0.8 ppb of SO_2 (IQR) significantly increased HR for suicide mortality; 3.09 (95% CI: 2.63–3.63); 1.33 (95% CI: 1.09–1.64); and 1.15 (95% CI: 1.07–1.24) respectively (Min *et al.,* 2018). Generally, compared to the lowest concentration of air pollutants, the risk of suicide significantly increased in the highest concentrations [PM_{10}: adjusted HR = 4.03 (95% CI: 2.97–5.47); NO_2: adjusted

HRs = 1.36 (95% CI: 1.02–1.83); and SO_2: adjusted HR = 1.65 (95% CI: 1.29–2.11)] (Min *et al.,* 2018). The association between these pollutants and suicide appeared to have a larger effect on subjects with a physical or mental disease than those without. Since, an association was found for all pollutants in those with a physical or mental disorders [PM10: HR = 3.27 (95% CI: 2.60–4.10); NO2: HR = 1.39 (95% CI: 1.03–1.87); and SO2: HR = 1.19 (95% CI: 1.07–1.33)] and only for PM_{10} in those without (HR = 2.81; 95% CI: 2.26–3.49) (Min *et al.,* 2018). Due to a lack descriptive statistics, information on how suicide was measured and lack of detail in the methods of the studies by Sun and Gładka they were described as low quality. Whereas the high-quality study by Min and colleagues, had 8-year follow-up period, large sample, suicide was diagnosed by ICD-10, and adjustment for demographic (age, sex, residential area, and household income), health behaviours (exercise, smoking, and alcohol consumption), disease status (physical or mental disease), and metrological (temperature and precipitation) variables.

Two ecologic time-series studies conducted in Mexico City (Astudillo-García *et al.,* 2019) and Columbia (Fernández-Niño *et al.,* 2018) did not find a significant statistical association between previous seven-day exposure to pollutants ($PM_{2.5}$, PM_{10}, O_3, NO_2, SO_2, CO) and suicide. The incidence rate ratios (IRR) for an increase in each pollutant were 0.97 (CI 95% 0.95-0.99) per 6 ppb of NO_2, 0.99 (CI 95% 0.99-1.00) per 1 ppb of SO_2, 0.99 (CI 95% 0.98-1.00) per 15 ppb O_3, 1.01 (0.99-1.02) per 10 μg/m^3 of PM_{10} and 0.99 (CI 95% 0.98-1.01) per 5 μg/m^3 of $PM_{2.5}$ (Astudillo-García *et al.,* 2019). Similarly, the IRR was 0.99 (95% CI: 0.95–1.04) per 6 μg/m^3 of NO_2, 0.99 (95% CI: 0.98–1.01) per 2 μg/m^3 of SO_2, 0.99 (95% CI:0. 95–1.03) per 10 μg/m^3 of PM_{10}, 1.01 (95% CI: 0.98–1.05) per 5 μg/m^3 of $PM_{2.5}$, 1.00 (95% CI:1.00–1.00) per 0.4 μg/m^3 of CO and 1.00 (95% CI: 0.96–1.04) per 10 μg/m^3 of O_3 (Fernández-Niño *et al.,* 2018). These associations were not found to be statistically significant after stratifying by sex and age group neither in lagged nor cumulative effects (Fernández-Niño *et al.,* 2018). Another time-series study in South Korea also found no significant association for the pollutants (NO_2, CO, SO_2) (Kim *et al.,* 2015). However, positive significant associations were found for O_3 and PM_{10} and suicide rate (Kim *et al.,* 2015). The greatest magnitude of the effect for O_3 was at lag 0. An increase in O_3 concentration of 0.016 ppm increased the weekly suicide rate by 7.8% of the national weekly rate (55.81 per 10 million from January 2006-December 2011) (Kim *et al.,* 2015). The most prominent effect of PM_{10} occurred with a four-week interval, when 37.82 μg/m^3 increase corresponded to a weekly suicide rate increase of 2.03 per 10 million or 3.6% of the national weekly suicide rate of 55.81 per 10 million (Kim *et al.,* 2015).

All three studies were classified as moderate quality. Two of the studies only adjusted for meterological variables (temperature and humidity) (Fernández-Niño *et al.,* 2018; Astudillo-García *et al.,* 2019) and the other study also adjusted for celebrity suicides and economic variables (consumer price index, unemployment rate, and stock index valuations) (Kim *et al.,* 2015). There was no adjustment or consideration of previous mental health or individual variables such as age, income, and sex. These studies also lacked descriptive statistics such as age and sex, although these were long-term studies which looked at various pollutants.

Six time-stratified case-crossover studies investigated exposure to air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, CO) up to seven days before and on the day of the suicide mortality in a Chinese city (Lin *et al.,* 2016), South Korean cities (Lee *et al.,* 2018), Tokyo (Ng *et al.,* 2016), Belgium (Casas *et al.,* 2017), Utah (Bakian *et al.,* 2015) and in Northeast Asian cities (Kim *et al.,* 2018).

Two studies explored same day and previous 7-day exposure (Lin *et al.,* 2016; Lee *et al.,* 2018). Significant associations were found on the same day (lag 0) for increases in all pollutants. The percent change in ORs were; PM_{10} 31.5 μg/m^3: 1.2% [95% CI, 0.2%-2.3%], NO_2 17 ppb: 4.3% [95% CI, 1.9%, 6.7%]; SO_2 3.1 ppb: 2.2% [95% CI, 0.7%, 3.8%]; O_3 21.2 ppb: 1.5% [95% CI, −0.3%, 3.2%]; and CO 0.32 ppm: 2.4% [95% CI, 0.9%, 3.8%] (Lee *et al.,* 2018). In subgroup analyses, stronger associations were observed in males (from 2.3% [95% CI, 0.7%, 3.8%] for CO to 4.5% [95% CI, 1.8%, 7.2%] for NO_2), the elderly (≥65 years) (from 4.0% [95% CI, 1.4%, 6.7%] for CO to 6.1% [95% CI, 2.5%, 9.8%] for NO_2) and those with lower education status (from 3.5% [95% CI, 1.0%, 6.0%] for CO to 6.2% [95% CI, 1.1%, 11.5%] for NO_2) (Lee *et al.,* 2018). Lin *et al*. (2016) found significant positive associations of suicides with IQR increases (not stated) in the pollutants: PM_{10} (ORs 1.13 [95 % CI: 1.01, 1.27] at lag0–2), NO_2 (ORs 1.15 [95 % CI: 1.03, 1.28] at lag0–2), and SO_2 (ORs 1.12 [95 % CI: 1.02, 1.23] lag0–1). Greater effects were observed in males and people with high education level than for females and those with low education level. In addition, statistically significant effects of SO_2 and NO_2 in people less than 65 years old but not in the elderly. Significant effects were found on violent suicide mortality and in cool season but not on non-violent suicide mortality or in the warm season (Lin *et al.,* 2016).

Two studies investigated exposure same day and 3 days before the suicide (Bakian *et al.,* 2015; Ng *et al.,* 2016). The maximum heightened odds of suicide were associated with IQR increases in NO_2 during the 3 days preceding suicide (cumulative lag 3); (OR = 1.20, 95% CI: 1.04, 1.39) and $PM_{2.5}$ on day 2 before suicide (lag 2); (OR = 1.05, 95% CI: 1.01, 1.10) (Bakian *et al.,* 2015). The association was also significant for NO_2 on lag 2 and 3. No significant association for PM_{10} and SO_2 as the ORs passed through zero. Although, for PM_{10} the odds of suicide increased with longer exposure but for SO_2 the coefficients were close to zero. Increased risk of suicide associated with NO_2 and $PM_{2.5}$ was strongest among males as well as 36–64-year-olds at lag 3 and during cumulative lags 2-3 for NO_2 and lag 2 for $PM_{2.5}$ (Bakian *et al.,* 2015). However, Ng *et al*. (2016) found no significant association with suicides and $PM_{2.5}$, suspended particulate matter (SPM), SO_2, and NO_2. All coefficient values were approximately zero. Apart from in those aged less than 30 years old (percentage change: 6.73%, 95% CI: 0.69–13.12%) for 13.9 ppb increase in NO_2 at lag0 and widowed subjects (10.55%, 95% CI: 2.05–19.75%) and (11.47%, 95% CI: 3.60–19.93%) for 11.0 μg/m^3 in $PM_{2.5}$ and 1.9 ppb in SO_2 respectively at lag0-3.

A study by Casas and colleagues found significant positive associations which varied by the season. During summer a 6–7% statistically significant increase in the odds of suicide was observed for 10 μg/m^3 increases of PM_{10} (interaction p-value <0.1 for lags 0–4) (Casas *et al.,* 2017). Whereas O_3 concentrations were significantly associated with suicide mortality throughout the study period, with positive associations in all seasons (interaction p-values <0.05 for lags 0–2 to 0–6) except winter, for which significant inverse associations were observed (lags 0–5 and 0–6) (Casas *et al.,* 2017). The ORs during summer for PM_{10} and O_3 with suicide ranged from 1.02 [2% increase in odds] to 1.07 [7% increase in odds] (p-values=0.05) (Casas *et al.,* 2017). Age significantly modified the associations with PM_{10}, with statistically significant associations observed only among 5–14-year-old children (lag 0–6: OR = 1.45; 95% CI: 1.03–2.04) and ≥85-year-olds (*e.g.,* lag 0–4: OR = 1.17; 95% CI: 1.06–1.29) (Casas *et al.,* 2017). In ten cities in South Korea, Japan, and China higher risk of suicide was significantly associated with higher levels of NO_2, SO_2 and PM_{10} over multiple days (Kim *et al.,* 2018). The combined RRs were for increases in the 0–1-day average level of each pollutant: 1.019 (95% CI: 0.999, 1.039) per 14.1 ppb of NO_2, 1.020 (95% CI: 1.005, 1.036) per 4.3 ppb SO_2 and 1.016 (95% CI: 1.004, 1.029) per 36.4 μg/m^3 PM_{10} (Kim *et al.,* 2018). The association was non-significant per 16.9 μg/m^3 increase in $PM_{2.5}$ [1.0017 (95% CI: 0.97, 1.058)] (Kim *et al.,* 2018). Some of the associations, particularly for SO_2 and NO_2, were attenuated after adjusting for a second pollutant. There was no clear pattern of effect modification by sex nor age and the confidence intervals among the subgroups largely overlapped covering the point estimates, suggesting that large uncertainty exists when comparing estimates across the groups (Kim *et al.,* 2018).

All time-stratified case-crossover studies were described as moderate to high quality. Since the study design controls for time-invariant individual characteristics such as sex and genetic predisposition as well as slowly varying characteristics such as age, marital/employment status, and seasonality can be controlled by selecting control days close to the case day. These studies also adjusted for various meterological and time variables (for example day-of-the-week, sunshine, temperature, humidity). However, one of the limitations was previous mental health diagnoses or treatment were not accounted for. Since, when investigating suicide, considering mental health history is important as psychiatric disorders such as depression, substance use disorders and psychosis are important risk factors (Backman, 2018). Moreover, psychological factors which are risk factors for suicide are difficult to control or adjust for such as life events (bereavement[s]) or lack of compliance to mental health treatment as well as poor social support. Other than Bakian and colleagues who retrieved the suicide information from a medical examiner where there could be miss clarification, all other studies defined suicide with an ICD-10 diagnosis. Although, suicide is underreported which could affects the results (Katz et al., 2015). In the studies fixed monitors were used so the accuracy of individual exposure estimates could be reduced (Briggs *et al.,* 1997; Briggs, 2005).

The information in this section is summarised in **Tables 2.10** and **2.11** below.

2.3.3.4 Summary of Suicide Related Mental Health Outcomes and Pollution Associations

The associations between suicide related mental health outcomes and air pollutants investigated in the above section are summarised in the **Table 2.10** below.

Table 2.10- Summary of the associations found between various pollutants and suicide.

Pollutant exposure & source	Association of Pollutants with Suicide	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Positive:**			Positive associations were found in five studies and no association was found in four studies. Therefore, further clarity is needed via large high-quality studies.
	Attempts	(Aguglia *et al.*, 2021)	Low correlation (32%)	
	Mortality	(Sun *et al.*, 2020)	Low correlation (0.577)	
	Significant positive:			
	Mortality	(Bakian *et al.*, 2015)	Strongest in males & 36–64-year-olds.	
		(Gładka *et al.*, 2021)	0.55 increase in rate	
	Ideation	(Luo *et al.*, 2020)	ORs 1.10 per μg/m^3	
	No association	(Ng *et al.*, 2016)	Coefficients close to zero.	
		(Kim *et al.*, 2018)		
		(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		
PM_{10}	**Significant positive:**			Significant positive associations were found in eight studies and
	Ideation	(Luo *et al.*, 2020)	ORs 1.05 per μg/m^3	

	Mortality	(Kim *et al.*, 2015)	3.6% of the national weekly rate per 37.82 μg/m^3	three found no association. PM_{10} could be a risk factor however more research is needed. Particularly research into covariates.
		(Lin *et al.*, 2016)	ORs 1.13. Greater effects in males & people with high education level.	
		(Casas *et al.*, 2017)	6–7% increase per 10 μg/m^3 in summer.	
		(Lee *et al.*, 2018)	1.2% per 31.5 μg/m^3. Stronger associations in males, ≥65 & those with lower education.	
		(Kim *et al.*, 2018)	Low RR 1.016.	
		(Min *et al.*, 2018)	Highest HR 3.09 for all subjects.	
		(Gładka *et al.*, 2021)	0.54 increase in rate	
	No association	(Bakian *et al.*, 2015)	Coefficients close to 1 or 0.99.	
		(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		
NO_2	**Significant positive:**			NO_2 could be a potential risk factor for suicidality as six studies found a significant association. This pollutant also had the highest OR compared to the other
	Ideation	(Luo *et al.*, 2020)	Highest OR 1.12	
	Mortality	(Bakian *et al.*, 2015)	Highest OR 1.20	
		(Lin *et al.*, 2016)	Highest OR 1.15	

		(Kim *et al.*, 2018)	Low RR 1.019	pollutants. Although, in one study only vulnerable populations were affected, and five studies found no association. Therefore, more research is required to clarify the association.
		(Lee *et al.*, 2018)	Highest OR 4.3% per 17 ppb.	
		(Min *et al.*, 2018)	In people with physical or mental disorders.	
	No association	(Kim *et al.*, 2015)	Coefficients close to zero.	
		(Ng *et al.*, 2016)		
		(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		
SO_2	**Significant positive**	(Lin *et al.*, 2016)	ORs 1.12 at lag0-1	Despite, four studies finding a significant association, five did not. SO_2 may not be an important risk factor. Although, more research is necessary to confirm this.
		(Lee *et al.*, 2018)	2.2% per 3.1 ppb	
		(Kim *et al.*, 2018)	Low RR 1.020	
		(Min *et al.*, 2018)	In people with physical or mental disorders.	
	No association	(Bakian *et al.*, 2015)		
		(Kim *et al.*, 2015)		
		(Ng *et al.*, 2016)		

		(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		
O_3	**Significant positive**	(Kim *et al.*, 2015)	7.8% of the national weekly rate per 0.016 ppm.	Three studies found a significant positive association and two did not find an association. Due to the lack of research, it is difficult to come to any conclusions.
		(Casas *et al.*, 2017)	All seasons apart from winter	
		(Lee *et al.*, 2018)	1.5% per 21.2 ppb	
	No association	(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		
CO	**Significant positive**	(Lee *et al.*, 2018)	2.4% per 0.32 ppm	Only one study showed a significant positive association and three found no association. So, CO may not be an important risk factor for psychotic disorders. Although, more research is necessary to confirm this.
	No association	(Kim *et al.*, 2015		
		(Fernández-Niño *et al.*, 2018)		
		(Astudillo-García *et al.*, 2019)		

- Positive associations and no association were demonstrated for all pollutants.
- The pollutants, PM_{10} and NO_2, could be risk factors for suicidality.

The quality assigned to the studies in this section is summarised in the **Table 2.11** below.

Table 2.11- Study quality described in the table below.

Quality	**Study Citation**
Low	(Sun *et al.,* 2020 Gładka *et al.,* 2021)
Moderate	(Kim *et al.,* 2015; Fernández-Niño *et al.,* 2018; Astudillo-García *et al.,* 2019; Aguglia *et al.,* 2021)
Moderate to high	(Bakian *et al.,* 2015; Lin *et al.,* 2016; Ng *et al.,* 2016; Casas *et al.,* 2017; Kim *et al.,* 2018; Lee *et al.,* 2018)
High	(Min *et al.,* 2018; Luo *et al.,* 2020)

2.3.4 Mania

Only one paper had an outcome of mania (Carugno *et al.,* 2021). The data extraction table for mania is linked here. Mania is often a symptom of bipolar and consists of elevated or irritable mood, over-activity, rapid speech, and a decreased need for sleep (WHO, 2022). A manic episode with mixed features, is when an individual feels both high and low emotions. The study population consisted of individuals diagnosed with mania by psychiatrists using the Structured Clinical Interview for DSM-IV axis I Disorders (SCID-I) (Carugno *et al.,* 2021). Manic episode severity was measured using the Young Mania Rating Scale (YMRS) at hospital admission (Carugno *et al.,* 2021). Higher scores using YMRS represented more severe symptoms. The study design was cross-sectional and conducted in a hospital in Milan using clinical records from 2007-2019. The effects of PM_{10} exposure from the day of mania admission (lag 0) up to 7 days before (lag 7) were investigated.

Short-term PM_{10} exposure was associated with a reduction in manic episode severity, when considering daily lags (β: − 0.43 [95% CI: − 0.83; − 0.03] at lag0) and their average (− 0.47 [− 0.90; − 0.04] at lag0-1) (Carugno *et al.,* 2021). Moreover, no association was observed between PM_{10} levels and the risk of being hospitalized for a manic episode with psychotic features (Carugno *et al.,* 2021). However, a 10 $\mu g/m^3$ increase in PM_{10} was associated with higher risk of a manic episode with mixed features [OR 2.43 (95%CI: 1.02; 5.76) and 2.50 (95%CI: 1.03; 6.08) at lags 0 and 1, respectively] (Carugno *et al.,* 2021). An even higher effect was observed when considering averaged daily lags 0-1 to 0-3, with OR ranging from 3.07 (95%CI: 1.18; 8.00) at lag 0-1 to 3.60 (95%CI: 1.22; 10.7) at lag 0-2 (Carugno *et al.,* 2021). These associations were not changed by individual characteristics (*i.e.,* age at hospitalization, sex, and smoking habit).

These results are not generalisable since one study had an outcome of mania, the effects of only one pollutant were investigated and data was only from one hospital. Furthermore, the cross-sectional design creates difficulties establishing a clear cause–benefit relationship. However, Carugno and colleagues, gave a detailed account of how air pollution and manic episodes were measured and adjusted for age at hospitalization, sex, smoking habit, year of hospitalization, season, and apparent temperature. However, important factors such as deprivation and socioeconomic status were not included. Therefore, overall, the study was described as a moderate quality. The information in this section is summarised in **Table 2.12** below.

2.3.4.1 Summary of Mania and Pollution Associations

The associations between mania and PM_{10} investigated in the above section are summarised in **Table 2.12** below.

Table 2.12- Summary of the associations found between PM_{10} and mania.

Pollutant exposure and source	The Association of Pollutant with Mania	Reference	Key Findings	Conclusions
Short-term PM_{10}	**Positive** with mixed episodes.	(Carugno *et al.,* 2021)	Age, sex & smoking status had no effect.	PM_{10} could have a potential depressogenic effect
	Negative with manic episode severity		Higher risk with longer periods of exposure.	Only one study so further clarity is needed by future research.
	None with mania symptoms or manic episodes with psychotic features.			

- More research is necessary to confirm which pollutants if any are risk factors for mania.
- This study was described as moderate quality.

2.3.5 Self-harm

Overall, two studies had an outcome of self-harm (Liu *et al.,* 2018; Mok *et al.,* 2021). The data extraction table for self-harm is linked here. Self-harm was defined by Function of Self-Mutilation (FASM) measure within the National Youth Health Risk Behaviours questionnaire (Liu *et al.,* 2018). Mok *et al*. (2021) defined self-harm in multiple ways:

1. Psychiatric diagnosis (ICD-10) and a comorbid diagnosis of poisoning, excluding alcohol and food poisoning (ICD-10) and lesions on forearm, wrist, or hand.
2. Hospital contacts due to poisoning with analgesics, hypnotics, sedatives, psychoactive drugs, anti-epileptics and anti-Parkinson drugs or carbon monoxide.
3. Primary or secondary diagnosis of intentional self-harm (ICD-10).

The pollutants studied were $PM_{2.5}$ and NO_2 (Mok *et al.,* 2021) as well as multiple pollutants ($PM_{2.5}$, CO, NO_2, O_3, SO_2) (Liu *et al.,* 2018). Both studies investigated long-term exposure. Annual exposure in a Chinese province (Liu *et al.,* 2018) and from birth until their 10th birthday at their residence in Denmark (Mok *et al.,* 2021).

Liu and colleagues conducted a cross-sectional study investigating self-harm and pollution levels in students at middle and high school as well as college (8-24). The pollutants, $PM_{2.5}$, O_3 and CO were significantly positively correlated with self-harm incidence (Liu *et al.,* 2018). Whereas no association was found for SO_2 and NO_2. An increase of 10 µg/m^3 in $PM_{2.5}$ and O_3 was associated with 13.9% and 10.5% higher odds of self-harm respectively (Liu *et al.,* 2018). A 0.1 mg/m^3 increase of CO was associated with 5.1% higher odds of self-harm (Liu *et al.,* 2018). The most susceptible group to self-harm after $PM_{2.5}$ exposure were male high school students with relatively low mother's education (Liu *et al.,* 2018). However, O_3 and CO were significantly associated with self-harm in all middle and high school students, regardless of sex, mother's education, and maltreatment (Liu *et al.,* 2018). The concentration-response relationship for $PM_{2.5}$ was linearly correlated with the risk of self-harm, while O_3 and CO were not linearly correlated (Liu *et al.,* 2018). For male high school students with lower mother's education (high-risk population), the ORs for self-harm increased as the average concentration of all three pollutants increased (Liu *et al.,* 2018). The OR for self-harm in the highest $PM_{2.5}$ quartile was (1.98-fold [95% CI: 1.54-2.54]) higher than in the lowest quartile (Liu *et al.,* 2018). A similar trend was found for CO, the highest OR was found in the highest quartile (1.43 [95% CI: 1.28-1.61]) (Liu *et al.,* 2018). Although, for O_3, the highest OR appeared at the third quartile (1.23 [95% CI: 1.06-1.42]) (Liu *et al.,* 2018).

Mok and colleagues, conducted a cohort study of the effects of childhood (0-10 years old) exposure on future self-harm risk. Increases in exposure to both $PM_{2.5}$ and NO_2 had a significant ($p < 0.001$) association to self-harm risk. For every 5 µg/m^3 elevation in mean daily $PM_{2.5}$, there was 1.42 times (95% CI 1.36–1.49) increased self-harm risk (Mok *et al.,* 2021). The IRR was slightly reduced for NO_2. For every 10 µg/m^3 elevation in mean daily NO_2, there was 1.21 times (95% CI 1.17–1.24) increased self-harm risk (Mok *et al.,* 2021). A dose relationship was most evident between increasing $PM_{2.5}$ and rising self-harm risk. Those exposed to the highest $PM_{2.5}$ concentrations, 19 µg/m^3 or above on average per day from birth to 10th birthday had 1.59 times (1.45–1.75) elevated self-harm risk whilst exposure to 17–19 µg/m^3 was associated with a 1.45-fold (95% CI 1.37–1.53) elevated risk compared with <13 µg/m^3. Associations were attenuated for $PM_{2.5}$ but increased for NO_2 after adjustment for parental mental illness, socioeconomic position, and urbanization level, although they remained significantly elevated (Mok *et al.,* 2021). The IRR per 5 µg/m^3 increase in $PM_{2.5}$ was attenuated from 1.42 (95% CI 1.36–1.49) to 1.35 (95% CI 1.27–1.43). Whereas the IRR per 10 µg/m^3 increase in NO_2 was increased from 1.21 (95% CI 1.17–1.24) to 1.24 (95% CI 1.19–1.28).

Both studies were described as high quality because of their large samples, multiple pollutants were investigated, clear methodology, as well as adjustment for demographic and social variables *e.g.,* sex, socioeconomic position, and maltreatment. Mok *et al.* (2020) additionally adjusted for parent's mental illness which is important because findings show children who experience poor parental mental health have consistently greater distress compared to those that do not (Kamis, 2020). Moreover, the self-harm cohort in Mok *et al*. (2020) study is likely to be representative as data was obtained through various methods and secondary diagnoses of self-harm were considered.

The information in this section is summarised in **Tables 2.13** and **2.14** below.

2.3.5.1 Summary of Self-harm and Pollution Associations

The associations between self-harm and various pollutants investigated in the two studies above are summarised in **Table 2.13** below.

Table 2.13- Summary of the associations found between various pollutants and self-harm.

Pollutant exposure & source	Association of Pollutant with Self-harm	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Positive significant**	(Liu *et al.*, 2018)	13.9% higher odds per 10 µg/m^3. Most susceptible to higher concentrations were male high school students with low mother's education.	$PM_{2.5}$ could increase the risk of self-harm. More research is needed clarify this association and the factors that could affect it.
		(Mok *et al.*, 2020)	IRR 1.42 increase per 5 µg/m^3. Association reduced by adjustment for socio-economic position, parental mental health & childhood urbanization level.	
NO_2	**Positive significant**	(Mok *et al.*, 2020)	IRR 1.21 increase per 10 µg/m^3. Reduced compared to $PM_{2.5}$. Association increased after adjustment socio-economic position, parental mental health & childhood urbanization level.	Further research is needed due to lack of research. However, the effects were reduced compared to $PM_{2.5}$.
	No association	(Liu *et al.*, 2018)		
O_3	**Positive significant**	(Liu *et al.*, 2018)	10.5% higher odds per 10 µg/m^3. Less of a dose response relationship compared to $PM_{2.5.}$ Not effected by confounders.	Only one study found so further clarity is needed through research.

CO	**Positive significant**	(Liu *et al.,* 2018)	5.1% higher odds per 0.1 mg/m^3. Not effected by confounders.	Further research is necessary.
SO_2	**No association**	(Liu *et al.,* 2018)		Further research is necessary.

- $PM_{2.5}$ could be a risk factor for self-harm, but further clarity is necessary through research evidence.

The quality assigned to the studies in this section is summarised in **Table 2.14** below.

Table 2.14- Study quality described in the table below.

Quality	Study Citation
High	(Liu *et al.,* 2018; Mok *et al.,* 2021)

2.3.6 Anxiety

In total 14 studies had an outcome of anxiety. The data extraction table for anxiety is linked here. Seven studies had an outcome of anxiety symptoms which were self-reported using different scales and questionnaires:

- **Spence Children's Anxiety Scale (SCAS)** in two studies (Brunst *et al.,* 2019; Yolton *et al.,* 2019),
- **State Anxiety Inventory for children (SAIC)** in one (Choi *et al.,* 2020),
- **Generalized Anxiety Disorder-2 (GAD-2)** scale in two studies (He *et al.,* 2021; Shi *et al.,* 2020),
- **Hospital Anxiety and Depression Scale (HADS)** in one study (Pun *et al.,* 2017). HADS is used in hospital medical outpatient clinics to reliably detect anxiety and depression symptoms (Zigmond & Snaith, 1983).
- **Crown-Crisp index phobic anxiety scale** in one study (Power *et al.,* 2015)

In five studies anxiety was diagnosed using ICD-10 (Cho *et al.,* 2015; Yue *et al.,* 2020; Zhao *et al.,* 2020; Ma *et al.,* 2021) and ICD9-CM (Kuo *et al.,* 2018). One study measured anxiety symptoms at age 12 using the Multi-dimensional Anxiety Scale for Children (MASC) and then re-interviewed the same individuals using DSM-IV at 18 years-old (Roberts *et al.,* 2019). Another study used the semi-structured Composite International Diagnostic Interview according to DSM-IV criteria and measured anxiety severity using the 21-item Beck Anxiety Inventory (Generaal *et al.,* 2019). In terms of the pollutants studied, eight studies, investigated various sizes of PM:

- $PM_{2.5}$ (Choi *et al.,* 2020; Generaal *et al.,* 2019; Pun *et al.,* 2017) and its constituents (Shi *et al.,* 2020)
- PM_{10} (Kuo *et al.,* 2018; Zhao *et al.,* 2020)
- PM_{10} and $PM_{2.5}$ (Power *et al.,* 2015; Yue *et al.,* 2020)
- PM_1 (He *et al.,* 2021)

In the other studies, two investigated multiple pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3 and CO) (Cho *et al.,* 2015; Ma *et al.,* 2021), two studies focused on traffic related air pollution (Brunst *et al.,* 2019; Yolton *et al.,* 2019) and one study explored NO_2 and $PM_{2.5}$ (Roberts *et al.,* 2019).

2.3.6.1 Symptoms

Altogether, seven studies had an outcome of anxiety symptoms. Three of the studies investigated long-term exposure, 5-year exposure (Brunst *et al.,* 2019) and annual exposure (Yolton *et al.,* 2019) to traffic related pollution as well as 3-year exposure to PM_1 (He *et al.,* 2021). Two cohort studies conducted in the US found children exposed to Elemental Carbon Attributable to Traffic (ECAT) were associated with anxiety symptoms (Brunst *et al.,* 2019; Yolton *et al.,* 2019). Children exposed to higher previous year ECAT levels at age 12 reported significantly more generalized anxiety symptoms (β =

4.71; 95% CI 0.95, 8.45) compared to children exposed to lower ECAT (Brunst *et al.,* 2019). Non-significant positive associations were found between ECAT exposure at birth (β = 1.64; 95% -2.27, 5.55) and average childhood (β = 2.81; 95% -0.95, 6.57) (Brunst *et al.,* 2019). Similarly, Yolton and colleagues found a 0.25 $\mu g/m^3$ increase in ECAT exposure in childhood and current exposure (at age 12) was significantly associated respectively with 3.26-point (95% CI 0.99, 5.53) and 2.47 (95% CI 0.55, 4.39) increase in generalized anxiety score. ECAT exposure during their childhood and at age 12 also significantly increased social phobia (β = 3.32, 95% CI 0.85, 5.79) (β = 2.51, 95% CI 0.43, 4.59) (Yolton et al., 2019). Contrastingly, anxiety score and PM_1 concentration were not correlated (Spearman's rank coefficient= − 0.05, P < 0.001) in a cross-sectional study in China (He *et al.,* 2021).

These studies were described as moderate to high-quality because they adjusted for maternal depression, parental relationship, and socioeconomic status (Brust *et al.,* 2019; Yolton *et al.,* 2019). Additionally, He *et al*. (2021) adjusted for health behaviours (physical activity, smoking status, drinking status, diet), history of chronic diseases, sex, education level, occupation, and income. All studies had large cohorts, described the participants' characteristics (sex/age) and used validated questionnaires described in research as reliable (Spitzer *et al.,* 2006; Orgilés *et al.,* 2016). However, various pollutants were not investigated, instead more specific types (PM_1 or traffic related carbon).

Two studies explored the effects of short-term $PM_{2.5}$ exposure, two-week averages (Shi *et al.,* 2020) and daily exposure (Choi *et al.,* 2020). In a Korean panel study, no association was found between $PM_{2.5}$ exposure and anxiety in children during the study period (β= − 0.19, SE=0.16, *p*-value= 0.24 in the adjusted model) (Choi *et al.,* 2020). Although, a cross-sectional study of older individuals (average age 62.7 ± 13.5) conducted in Chinese cities found a 39.2 $\mu g/m^3$ (IQR) increase in $PM_{2.5}$ was associated with an OR of 1.60 (95% CI: 0.99, 2.58) for anxiety (Shi *et al.,* 2020). The ORs for anxiety varied by constituent. Anxiety was significantly associated with the 2-week moving average concentrations of organic carbon (OC), elemental carbon (EC), copper (Cu), zinc (Zn), and nickel (Ni). The ORs of EC and Ni were the highest, at 1.48 (95% CI: 1.11, 1.98) and 1.59 (95% CI: 1.18, 2.15) per 7.1 $\mu g/m^3$ and 10.1 ng/m^3 (IQR) increase, respectively (Shi *et al.,* 2020). Differences in age, sex, education level, BMI and season did not have significant effects (Shi *et al.,* 2020). These associations were also not affected by covariates and changing the anxiety cut-off.

The study by Choi and colleagues was described as moderate quality due to the short study period (3 months), small number of participants (57) and only one pollutant was investigated. However, exposure was measured in multiple locations (school, classroom and activity based) and there was adjustment for meterological (month, humidity, temperature), psychological (family history of psychological disease) and demographic variables (sex, household income, parents' ethnicity). However, the study by Shi and colleagues was classified as high-quality because the percentage of participants with anxiety was given, participants were described in detail, in terms of, household income, living with family, married or not, and chronic disease. In addition, GAD-7 scale is a reliable tool used in primary and secondary care. Moreover, there was adjustment for demographic variables (age, sex, education level, annual household income), health behaviours (smoking status, drinking status, BMI, and self-reported chronic diseases), psychological (social support level) and meteorological factors (temperature, humidity, and season [heating vs non-heating period]).

Two different longitudinal cohort studies conducted in the US explored the effects of short-and-long-term exposure to PM prior to the anxiety assessment. Length of exposure was one month to 15-years (Power *et al.,* 2015) and 7 days to 4-years (Pun *et al.,* 2017). Power and colleagues showed higher $PM_{2.5}$ and high anxiety across several averaging periods in older women. Over a shorter (12, 6, 3 and 1 month) period associations were similar and stronger compared to 1988–2003 exposure. The clearest dose response relationship was shown in the previous 1-month exposure model in which ORs increased as the concentration increased. The OR per 10 $\mu g/m^3$ increase in $PM_{2.5}$ during one-month was 1.12 (95% CI 1.06-1.19) (p=0.0001) and annually was 1.15 (95% CI 1.06-1.26) (p=0.001) (Power *et al.,* 2015). However, no association was found between anxiety and PM_{10} (Power *et al.,* 2015). No significant effect modification by demographic, geographic, or health related characteristics of the association with one-month $PM_{2.5}$ exposure (likelihood ratio test P>0.16 for all) (Power *et al.,* 2015). Pun and colleagues also found an association between anxiety risk and $PM_{2.5}$ over both short-and long-term exposure. The ORs for anxiety were significant (p<0.10) in all moving averages 7, 30, 180, 365 days and 4 years respectively 1.14 (95% CI 1.05-1.24), 1.31 (95% CI 1.20-1.51), 1.61 (95% CI 1.35-1.92), 1.39 (95% CI 1.15-1.69) and 1.34 (95% CI 1.12-1.61) (Pun *et al.,* 2017). Increased odds of moderate-to-severe anxiety symptoms were associated with $PM_{2.5}$ among individuals who had less than a high school education [1.97 (1.60, 2.41) p-interact < 0.001] and a history of stroke or heart failure compared to those without [1.55 (1.22, 1.98) p=0.002 or 1.97 (1.47, 2.63) p=0.007] (Pun *et al.,* 2017).

Both studies were described as moderate quality because of adjustment for socioeconomic status, education, ethnicity, region of residence, age, and the samples were large. However, only PM was considered despite the likelihood of other pollutants having an effect. In addition to a lack of clinical diagnosis and information on the activity pattern of each participant. Moreover, the cohort in the study by Power and colleagues consisted of only married female nurses which is not representative of the general population.

2.3.6.2 Diagnoses

Overall, five studies had an outcome of diagnosed anxiety (Cho *et al.,* 2015; Kuo *et al.,* 2018; Yue *et al.,* 2020; Zhao *et al.,* 2020; Ma *et al.,* 2021). Three investigated short-term exposure to multiple pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3 and CO), day of diagnosis and 3 days before (Cho *et al.,* 2015), 7 days before and after the event (Ma *et al.,* 2021) in time-series studies and 7 days before the event in a time-stratified case cross-over study (Yue *et al.,* 2020). One cross-sectional study investigated 10-year exposure to PM_{10} (Zhao *et al.,* 2020). Additionally, a time-series study investigated exposure at different PM_{10} concentrations and lengths respectively (< 35 for 625 days, 35–65 for 924 days, 66–125 for 1179 days, 126–300 for 190 days, 301–500 for 2 days and > 500 for 2 days) (Kuo *et al.,* 2018).

A time-series study conducted in Korea by Cho and colleagues, found only O_3 was significantly associated with emergency department visits for panic attacks. The RR was 1.051 (95% CI, 1.014-1.090) for same-day exposure and for cumulative lags the RRs were 1.059 (1.021-1.099) in lag 0-1, 1.068 (1.029-1.107) in lag 0-2, and 1.074 (1.035-1.114) lag0-3 (Cho *et al.,* 2015). This association varied by sex, presence of an underlying condition and season. Statistically significant results were found for women, those with diabetes mellitus and in summer (Cho *et al.,* 2015). Although, both sexes and during spring also increased the risk of panic attacks. However, SO_2, PM_{10}, NO_2, and CO were non-significantly associated with emergency department visits (Cho *et al.,* 2015). A time-series study conducted in 56 Chinese cities found short-term exposure to NO_2 and SO_2, were significantly associated with increased risk of daily anxiety hospital admissions (Ma *et al.,* 2021). A 10 µg/m^3 increase in NO_2 at lag0 and SO_2 at lag6 were associated with significant increases of 1.37% (95% CI: 0.14%- 2.62%) and 1.53% (95% CI: 0.59%- 2.48%) in anxiety admissions respectively (Ma *et al.,* 2021). Stronger associations were found in patients <65 years old for SO_2 only (Ma *et al.,* 2021). A 10 µg/m3 increase in SO_2 at lag01 was associated with significant increase of 2.65% (95% CI: 0.93%, 4.40%) in patients <65 years and an insignificant decrease of 0.59% (95% CI: − 2.64%, 1.51%) in patients ≥65 years old. However, associations by sex or age for NO_2 did not show significant differences. The relative risk for anxiety admissions appeared to be more significant at higher NO_2 and SO_2 concentrations, which was particularly evident for SO_2. Since for NO_2 significant findings were only at relatively high concentrations and became insignificant after controlling for SO_2 (Ma *et al.,* 2021). These associations were not affected by time and meterological variables. However, no association was found for $PM_{2.5}$, PM_{10}, O_3 and CO because the results had large confidence intervals and passed through zero (Ma *et al.,* 2021). In another study conducted in Chinese cities, positive associations were observed between $PM_{2.5}$ and PM_{10} concentrations and anxiety admissions at lag day 2, 3, 4, 5, 6, 0–2 including 0–5 days (Yue *et al.,* 2018). $PM_{2.5}$ had the largest effect estimate at lag 5 days, with a 10 μg/m^3 increase corresponding to a 0.63% (95% CI: 0.27–1.00, p=0.001) increase in anxiety admissions. The largest effect estimates for PM_{10} was observed at lag 3 days, when the rate of anxiety increased by 0.37% (95% CI, 0.12–0.62, p=0.004) per 10 μg/m^3. For PM_{10} there was a clearer exposure-response association between increases in concentration and risk compared to $PM_{2.5}$ at lag 5. In the two-pollutant model the percentage changes for PM concentrations at lag 0–5 reduced when adjusted for SO_2, NO_2 or CO, but associations and statistical significance did not change. Females were more sensitive to $PM_{2.5}$/PM_{10} than males at lag 0 and lag 0-2, however, the effect modification by age was non-significant. The percentage changes for $PM_{2.5}$ at lag 0 (males: 0.25%, 95% CI, −0.88-0.39; females: 0.61%, 95% CI, 0.15–1.07) and lag 0–2 day (males: 0.08%, 95% CI, −0.83 -0.68; females: 0.91%, 95% CI, 0.36–1.46) (P < 0.05). In terms of age a greater percentage change was shown in those aged ≥65 years than 18–64-year-olds at lag2, but the effects were not statistically significant (p=0.132). In Germany, a cross-sectional study demonstrated, anxiety hospital admissions were associated with 10 μg/m^3 increase in PM_{10} concentration with a RR of 1.18 (95% CI 1.15-1.21, p=0.00) (Zhao *et al.,* 2020). This was not affected by the inclusion of O_3 in the model (Zhao *et al.,* 2020). A time-series study in China also investigated exposure to different concentrations of PM_{10} and emergency department visits for panic disorder (Kuo *et al.,* 2018). Kuo and colleagues showed that as PM_{10} concentration increased so did daily clinic visits for anxiety. The largest increase in daily clinic visits was at 300 μg/m^3 (approximately >375 visits) to 301-500 μg/m^3 (>470 visits). When PM_{10} levels were 301-500 and >500 the association to anxiety was statistically significant compared to the lowest concentrations (<35 μg/m^3).

The study by Yue and colleagues was described as moderate to high quality because the time-stratified case-crossover design controls for time invariant confounders such as age and socioeconomic status as well as meterological variables (temperature, relative humidity, holidays). The other four studies were described as moderate quality. Cho *et al.* and Ma *et al.* did not adjust for socioeconomic, health and demographic variables. Moreover, these four studies assessed air pollution exposure with monitoring sites so individual exposure is unlikely to be very reliable (Briggs *et al.,* 1997; Briggs, 2005). However, all studies had a clinical diagnosis of anxiety and a large sample size.

2.3.6.3 Diagnostic Interview (DSM-IV) and Questionaire

Two studies used diagnostic interview and a questionaire to measure symptom severity (Generaal *et al.,* 2019; Roberts *et al.,* 2019).

In a cross-sectional study in the Netherlands, an anxiety diagnosis and annual $PM_{2.5}$ exposure were determined 1 year prior to the baseline interview using DSM-IV and anxiety severity scale (Generaal *et al.,* 2019). In the single analysis, high levels of $PM_{2.5}$ were significantly associated with anxiety diagnoses OR 1.21 (95% CI 1.04–1.41) (Generaal *et al.,* 2019). However, in the multivariable analysis, social security beneficiaries, traffic noise and water in the neighbourhood remained significantly associated with anxiety and higher home value became significantly associated OR 1.37 (95% CI 1.16–1.62) (Generaal *et al.,* 2019). Although, $PM_{2.5}$ was not associated with anxiety severity. When, in the multivariable analyses, all neighbourhood factors were combined, social security beneficiaries and traffic noise were significant (Generaal *et al.,* 2019). This study was described as a moderate/high quality study. The limitations were that only one pollutant was considered, the cross-sectional nature means it is not possible to establish a clear cause–benefit relationship and health or psychological variables were not considered. Although, age, sex, years of education and household income were adjusted for. Other advantages of the research were, anxiety was assessed using DSM-IV diagnostic manual, LUR models were used to estimate exposure, a large sample was used and a wide range of neighbourhood characteristics that could affect anxiety were considered (low neighbourhood socioeconomic status, high levels of traffic noise, less green space, more water in the neighbourhood, lower social cohesion, and less safety).

A longitudinal study in London, used a twin cohort to explore the effects of annual NO_2 and $PM_{2.5}$ exposure on anxiety symptoms at age 12, and then at 18 years old (Roberts *et al.,* 2019). No significant associations and effect sizes were small for coinciding associations between $PM_{2.5}$ and NO_2 exposure and anxiety symptoms at age 12 (Roberts *et al.,* 2019). For example, the coefficient for $PM_{2.5}$ was $\beta=-0.04$ (95% CI −0.19–0.11) and for NO_2 it was $\beta=-0.06$ (95% CI −0.20–0.09) (Roberts *et al.,* 2019). Additionally, no associations were found between estimated exposure to $PM_{2.5}$ or NO_2 at age 12 and an anxiety disorder diagnosis at 18 (all p's > 0.05) (Roberts *et al.,* 2019). The coefficient for $PM_{2.5}$ was $\beta=-0.01$ (95% CI 0.19–0.18) and for NO_2 it was $\beta=-0.01$ (95% CI −0.18–0.16) (Roberts *et al.,* 2019). No effect was found, despite, annualised NO_2 being above the current EU legislated standard for 31% of children (40 $\mu g/m^3$; also, the current WHO air quality guideline). Although, $PM_{2.5}$ was not above the EU standards.

The study by Roberts and colleagues was described as high-quality as the methods including how air pollution exposure and mental health were measured was clearly explained. In addition, there was adjustment for psychological variables (family psychiatric history, exposure to severe childhood victimization, age-12 mental health problems), demographic variables (sex, ethnicity, socioeconomic status), smoking status, and the non-independence of twin observations.

The information in this section is summarised in **Tables 2.15** and **2.16** below.

2.3.6.4 Summary of Anxiety and Pollution Associations

The associations between anxiety mental health outcomes and various pollutants investigated in the above section are summarised in **Table 2.15** below.

Table 2.15- Summary of the associations found between various pollutants and anxiety.

Pollutant exposure & source	Association of the Pollutant with Anxiety	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Significant positive** with diagnoses & symptoms	(Power *et al.,* 2015)	OR 1.12 per 10 μg/m^3 increase in 1-month exposure showed the strongest positive association & was not affected by covariates.	Long-term and short-term $PM_{2.5}$ exposure was associated with increased anxiety in four studies. However, four studies also did not find an association. Therefore, more research is necessary to clarify the effects of $PM_{2.5}$ on anxiety which also considers confounders such as socioeconomic status.
		(Pun *et al.,* 2017)	Highest OR 1.61 at 6-month exposure. Greater risk in those with lower education level & history of chronic disease.	
		(Yue *et al.,* 2018)	Largest effect at lag 5, 0.63% increase in anxiety admissions per 10 μg/m^3. Reduced when SO_2, NO_2 or CO were included. Females were more sensitive than males no age effects.	
		(Shi *et al.,* 2020)	OR 1.60 per 39.2 μg/m^3 in those aged 62.7 ± 13.5.	
	No association	(Roberts *et al.,* 2019)	In children β=−0.04 and adolescents β=−0.01.	

		(Choi *et al.,* 2020)	β= −0.19, p=0.24 in children.	
		(Generaal *et al.,* 2019)	Significant to anxiety in the single analysis. In multivariable analysis socioeconomic factors and traffic noise were.	
		(Ma *et al.,* 2021)		
PM_{10}	**Significant positive** with diagnoses	(Kuo *et al.,* 2018)	Significant at higher concentrations 301-500 & >500 µg/m^3 compared to low.	Significant positive associations were found in three studies and two studies found no association with anxiety diagnoses. Therefore, more research is required to elucidate the potential effects of air pollution on anxiety.
		(Yue *et al.,* 2018)	Largest effect at lag 3, 0.37% increase in admissions per 10 µg/m^3.	
		(Zhao *et al.,* 2020)	RR 1.18 per 10 µg/m^3 (10-year exposure).	
	No association to diagnoses	(Cho *et al.,* 2015)	Short-term daily lags. No adjustment for health & socioeconomic variables.	
		(Ma *et al.,* 2021)		
		(Power *et al.,* 2015)	Monthly to 15-year exposure.	
PM_1	**No association**	(He *et al.,* 2021)	Long-term exposure.	Lack of research means further clarity is needed into the effects of PM_1.
NO_2	**Significant positive** with diagnoses	(Ma *et al.,* 2021)	At lag 0 1.37% 10 per µg/m^3. Increased effects at higher concentrations.	Like the associations found for the above pollutants positive associations were found in one study however two studies found no association. The

	No association diagnoses	(Cho *et al.,* 2015)	Short-term (lag 0-3)	contrasting findings mean more research is needed.
		(Roberts *et al.,* 2019)	Long-term exposure in children β=−0.06 and adolescents β=−0.01.	
Short-term O_3	**Significant positive** with diagnoses	(Cho *et al.,* 2015)	Low RR (1.051) and significant for women, in summer & those with diabetes.	The lack of research combined with contrasting findings means further research is necessary.
	No association to diagnoses	(Ma *et al.,* 2021)		
Short-term SO_2	**Significant positive** with diagnoses	(Ma *et al.,* 2021)	At lag 6 1.53% 10 per μg/m^3. Increased effects at higher concentrations.	The lack of research combined with contrasting findings means further research is necessary.
	No association	(Cho *et al.,* 2015)		
Short-term CO	**No association**	(Cho *et al.,* 2015)		Carbon monoxide may not be a risk factor for anxiety however more research is required to confirm this.
		(Ma *et al.,* 2021)		
Long-term traffic related carbon	**Significant positive** with symptoms	(Brunst *et al.,* 2019)	More anxiety in high compared to low concentrations at age 12 (β = 4.71).	Increased concentrations of ECAT could be a risk factor for anxiety in children although more research is required.
		(Yolton *et al.,* 2019)	In childhood & age 12 0.25 μg/m^3 increase linked with 3.26- & 2.47-point increase in anxiety score.	

- Positive associations and no association were equally demonstrated for most pollutants.
- Therefore, it is difficult to come to conclusions.
- Although, the largest number of studies investigated $PM_{2.5}$ and found this pollutant could be a risk factor for anxiety.

The quality assigned to the studies in this section is summarised in **Table 18** below.

Table 2.16- Study quality described in the table below.

Quality	**Study Citation**
Moderate	(Cho *et al.,* 2015; Power *et al.,* 2015; Pun *et al.,* 2017; Kuo *et al.,* 2018; Choi *et al.,* 2020; Zhao *et al.,* 2020; Ma *et al.,* 2021)
Moderate/high	(Brunst *et al.,* 2019; Generaal *et al.,* 2019; Yolton *et al.,* Yue *et al.,* 2020; 2019; He *et al.,* 2021)
High	(Roberts *et al.,* 2019; Shi *et al.,* 2020)

2.3.7 Mortality Linked to Mental Illness/Well-being

Overall, four studies had an outcome of mortality linked to:

- Diagnosed **mental disorders** and **self-harm** (Li *et al.,* 2018)
- Diagnosed **self-harm** only (Li *et al.,* 2021)
- **Anxiety diagnoses** (Zock *et al.,* 2018).
- **Self-rated mental health**, **stress**, and **distress** (Thomson *et al.,* 2020)

The data extraction table for mortality linked to mental illness or well-being is linked here. Thomson and colleagues measured mental health and stress by asking participants to rate how good their mental health was and how stressful their days were. Distress was measured using Kessler Psychological Distress Scale (K6) (Thomson *et al.,* 2020). The outcomes were defined by ICD-10 diagnoses in China (Li *et al.,* 2018; Li *et al.,* 2021). In addition to, the linking of GP and mortality records in the Netherlands (Zock *et al.,* 2018). The pollutants investigated were:

- Multiple pollutants in differing combinations ($PM_{2.5}$, PM_{10}, NO_2, O_3, elemental carbon [EC], organic carbon [OC], NO_3^-) (Zock *et al.,* 2018; Li *et al.,* 2021; Thomson *et al.,* 2020).
- $PM_{2.5}$ in one study (Li *et al.,* 2018)

Two of the studies were conducted in two different Chinese cities and had a time-stratified case-crossover design. These explored exposure to $PM_{2.5}$ (Li *et al.,* 2018) and $PM_{2.5}$, EC, OC, NO_3^- (Li *et al.,* 2021) a week before mortality. The risk of mortality from self-harm increased by 1.94% (95% CI: 0.19%–3.73%) at lag of 0-1 per 10 μg/m^3 increase in $PM_{2.5}$ ($p<0.05$) (Li *et al.,* 2018). However, mortality risk from mental and behavioural disorders (− 0.35; 95%CI: − 2.19%–1.52%) were virtually unchanged with increasing $PM_{2.5}$ (Li *et al.,* 2018). In another study, the percentage change increases in self-harm were non-significant at lag 03 for increases in $PM_{2.5}$ 9.17% (− 4.87,25.27) per 38.4 μg/m^3, EC 2.15% (− 9.33,15.09) per 2.0 μg/m^3 and NO_3^- 0.56% (− 13.50,16.92) per 8.7 μg/m^3 (Li *et al.,* 2021). Although, the percentage change in self-harm mortality per 4.7 μg/m^3 increase in OC was significant 18.01% (95% CI: 2.14-36.36) at lag 03 (Li *et al.,* 2021). Both studies were described as moderate quality because their design controls for time and short-term time-invariant individual characteristics such as age. Meterological variables (temperature and humidity) were also controlled for. However, the limitations were exposure to only $PM_{2.5}$ was investigated (Li *et al.,* 2018) and the other study had a sample size of 7 (Li *et al.,* 2021).

A cross-sectional study in multiple Dutch cities investigated previous annual exposure to $PM_{2.5}$, PM_{10} and NO_2 effects on mortality linked to anxiety diagnoses. The ORs per 10 μg/m^3 increase were non-significant and positive 1.12 (0.40–3.12) for PM_{10} and 1.10 (0.91–1.33) for NO_2. However, for increases in $PM_{2.5}$ mortality risk reduced 0.32 (0.05–1.92) which was non-significant (Zock *et al.,* 2018). This study adjusted for sex, age, household income and socioeconomic status, considered multiple pollutants and described the study population in detail (age and sex). However, there was no adjustment for lifetsyle factor such as smoking, no information was given on cause of mortality and the study design means it is not possible to establish a clear cause–benefit relationship. Therefore, the study quality was described as moderate/high.

In the Canadian Community Health Survey mortality cohort, no differences were found in the stress- or distress-related hazard ratios (HR) for mortality due to $PM_{2.5}$, NO_2 and O_3 (Thomson *et al.,* 2020). In the unadjusted model, increases in the pollutants significantly elevated the risk of mortality in individuals with poor self-rated mental health compared to good or excellent mental health. For example, the unadjusted HR for non-accidental death linked to $PM_{2.5}$ was 1.10 (95% CI 1.04–1.17 per increase in 2.7 $\mu g/m^3$) for those with poor or fair self-rated mental health, compared to 1.02 (95% CI 1.00–1.04 per increase) for those with excellent or very good self-ratings (Cochran's Q = 5.68; $p < 0.05$). The magnitude of these differences tended to be maintained in the fully adjusted models and remained statistically significant only for NO_2. The HRs in the fully adjusted models for non-accidental mortality for NO_2 were 1.15 (95% CI 1.06–1.25 per 6 ppb) compared to those with very good/excellent mental health 1.05 (95% CI 1.01–1.08; Cochran's Q = 4.01; $p<0.05$). This study was moderate/high quality because:

- Air pollution and well-being were clearly defined.
- It had a large national cohort with socioeconomic, behavioural, and contextual data.
- Adjustment for demographic (sex, age, indigenous identity), socioeconomic (Marginalization Index, income) and behavioural factors (alcohol consumption, smoking behaviour, fruit and vegetable consumption, exercise).

However, self-rated well-being is also affected by individual stress reactivity (Thomas *et al.,* 2018) and specific stressors (Shmool *et al.,* 2015). Therefore, the questionaire used may not adequately capture the complexities of psychological stress. Additionally, there was a lack of descriptive statistics (age and sex).

The information in this section is summarised in **Tables 2.17** and **2.18** below.

2.3.7.1 Summary of Mortality Linked to Mental Health and Pollution Associations

The associations between mortality linked to mental health and various pollutants investigated in the above section are summarised in **Table 2.17** below.

Table 2.17- Summary of the associations found between various pollutants and mortality linked to mental health.

Pollutant exposure & source	Association with Mortality linked to Mental Health Outcomes	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Significant positive** to self-harm mortality	(Li *et al.*, 2018)	1.94% increase per 10 µg/m^3 lag0-1	Various mental outcomes or decreased mental health linked to mortality were investigated resulting in difficulties coming to conclusions. Moreover, some studies found worse mental health had links to mortality and other studies did not. Therefore, further research is required with consideration of covariates which are likely to have an impact on mortality.
	Positive association to:			
	Self-harm mortality	(Li *et al.*, 2021)	9.17% change per 38.4 µg/m^3 at lag03.	
	Mortality linked to worse self-reported mental health.	(Thomson *et al.*, 2020)	Only significant in unadjusted model.	
	No association with:			
	Mental disorders	(Li *et al.*, 2018)	− 0.35; 95% CI: −2.19%–1.52%	
	Stress/distress	(Thomson *et al.*, 2020)	No difference in HRs.	
	Non-significant with decreased odds of anxiety linked to mortality.	(Zock *et al.*, 2018)	OR 0.32 per 10 µg/m^3 increase	
PM_{10}	**Non-significant** increased anxiety linked to mortality.	(Zock *et al.*, 2018)	OR 1.12 per 10 µg/m^3 increase	Lacks research evidence.

NO_2	**Significant positive** to mortality linked to worse self-reported mental health.	(Thomson *et al.,* 2020)	In the adjusted & unadjusted model.	Various associations found in relation to different mental health outcomes and mortality. Therefore, further clarity through research is needed.
	Non-significant with **increased odds** of anxiety linked to mortality.	(Zock *et al.,* 2018)	OR 1.10 per 10 μg/m^3 increase	
	No association with stress/distress	(Thomson *et al.,* 2020)	No difference in HRs.	
NO_3^-	**Positive** for self-harm mortality.	(Li *et al.,* 2021)	0.56% change per 8.7 μg/m^3 at lag03.	Lacks research evidence.
OC	**Significant positive** to self-harm mortality.	(Li *et al.,* 2021)	18.01% change per 4.7 μg/m^3 at lag03.	Lacks research evidence.
EC	**Positive** to self-harm mortality	(Li *et al.,* 2021)	2.15% change per 2 μg/m^3 at lag03.	Lacks research evidence.
O_3	**Positive** to mortality linked to worse self-reported mental health.	(Thomson *et al.,* 2020)	Only significant in unadjusted model.	Likely that other factors (smoking or diet) could contribute to pollutant mortality relationships.
	No association with stress/distress		No difference in HRs.	

- Due to the variety of mental health outcomes and various confounders that are likely to affect the association between worse mental health and mortality (such as reduced physical health) it is difficult to come to any conclusions.

The quality assigned to the studies in this section is summarised in **Table 2.18** below.

Table 2.18- Study quality described in the table below.

Quality	**Study Citation**
Low/moderate	(Li *et al.,* 2018; Li *et al.,* 2021)
Moderate/high	(Zock *et al.,* 2018; Thomson *et al.,* 2020)

2.3.8 Self-reported Overall Mental Health and Well-being

In total three studies were considered to have an outcome of self-reported overall mental health and well-being. The data extraction table for these outcomes is linked here. Scales/questionnaires were used in all studies:

- **General Health Questionaire (GHQ)** (Dzhambov *et al.,* 2018)- usually consists of 12 items, each assessing the severity of a mental health problem over the past few weeks using a 4-point scale (from 0 to 3) (Luo *et al.,* 2004). The score is used to generate a total score ranging from 0 to 36, with higher scores indicating worse conditions (Luo *et al.,* 2004).
- **Symptom Checklist-90** (Chen at al., 2018a)- includes 90 symptoms and evaluates nine symptomatic dimensions: somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism (Sereda & Dembitskyi, 2016).
- **Five-item Satisfaction with Life Scale** (Chang *et al.,* 2019)- participants indicate how much they agree or disagree with each of the 5 items using a 7-point scale that ranges from 7 strongly agree to 1 strongly disagree.

The pollutants explored in the studies were:

- Multiple pollutants in one study AQI (Chang *et al.,* 2019)
- NO_2 only in one (Dzhambov *et al.,* 2018)
- $PM_{2.5}$ only in one study (Chen *et al.,* 2018a).

Three studies investigated short-term exposure, monthly AQI exposure (Chang *et al.,* 2019), $PM_{2.5}$ exposure a week prior to mental health assessment (Chen *et al.,* 2018a) and 2-month NO_2 exposure (Dzhambov *et al.,* 2018). A cross-sectional study in China found a positive relationship between AQI and life satisfaction (β=0.001) (Chang *et al.,* 2019). So, worse air quality was correlated with increased life satisfaction. In comparison, Chinese university students had significantly ($p< 0.01$) higher levels of positive symptom distress (PSD), obsessive-compulsive symptoms, interpersonal sensitivity, and psychoticism when $PM_{2.5}$ levels were higher (173.5 $\mu g/m^3$ compared to 16.1 $\mu g/m^3$) (Chen at al., 2018a). A cross-sectional study of Bulgarian medical students found no association between GHQ per 10 $\mu g/m^3$ increase in NO_2 (β=− 0.753 [95% CI−1.889, 0.383], *p*-value 0.194) (Dzhambov *et al.,* 2018). Although, NO_2 was associated with mental ill-health only indirectly through higher annoyance, lower restorative quality, and lower physical activity working in serial β=0.00003 (95% CI: 0.000001, 0.0001) *p*-value= 0.034 (Dzhambov *et al.,* 2018).

The study by Chen and colleagues was described as low-quality because in the initial assessment of mental health there were less participants compared to the follow-up and this was not addressed. Moreover, no information was provided on how air pollution was measured, and the study period was short. Although, some descriptive statistics were provided in terms of age and sex. Studies by Dzhambov *et al*. (2018) and Chang *et al*. (2019) were described as moderate quality. Since, only one pollutant was measured, and the study period was short. Although various confounding variables were measured and included in the statistics (age, sex, ethnicity, individual-level economic status, month of data collection, environmental annoyance, sleep disturbance, social cohesion, and physical activity) (Dzhambov *et al.,* 2018). However, Chang and colleagues did not consider health behaviours but did consider some demographic variables (age, sex, educational level, financial situation [self-rated]). Additionally, the study had a large sample (4627) although the reliability of the life satisfaction scale is uncertain (Chang *et al.,* 2019).

The information in this section is summarised in **Tables 2.19** and **2.20** below.

2.3.8.1 Summary of Self-reported Mental Health/Well-being and Pollution Associations

The associations between self-reported overall mental health/well-being and various pollutants investigated in the above section are summarised in **Table 2.19** below.

Table 2.19- Summary of the associations found between various pollutants and self-reported overall mental health.

Pollutant exposure & source	Association with Self-reported Mental Health/Well-being	Reference	Key Findings	Conclusions
Worse air quality	**Positive association:** with increased life satisfaction	(Chang *et al.*, 2019)	High pollutants levels had a positive effect on life satisfaction (β=0.001).	Air quality did not negatively impact life satisfaction. More research is needed to confirm this.
$PM_{2.5}$	**Significant positive** to worse mental health	(Chen at al., 2018a)	University students had worse well-being in 173.5 μg/m^3 compared to 16.1 μg/m^3.	$PM_{2.5}$ could negatively impact mental health, but more research is needed to clarify this.
NO_2	No association	(Dzhambov *et al.*, 2018)	Indirect association to mental health via higher annoyance, lower restorative quality, and lower activity.	Due to the lack of studies, it is difficult to estimate the potential impact, so more research is vital which considers covariates.

- Overall, the results may lack reliability and clinical significance as most of the associations were non-significant and mental health outcomes were self-reported through various questionnaires.
- Therefore, it is important that more research investigates subclinical mental health outcomes.
- However, the reliability of the outcomes needs to be considered and what symptoms are important to represent well-being and mental health.

The quality assigned to the studies in this section is summarised in **Table 2.20** below.

Table 2.20- Study quality described in the table below.

Quality	**Study Citation**
Low	(Chen at al., 2018a)
Moderate	(Dzhambov *et al.,* 2018; Chang *et al.,* 2019)

2.3.9 Self-reported Psychological Stress and Distress

Out of the eight studies in the stress and distress category, five measured psychological distress and six measured psychological stress. The data extraction table for stress or distress is linked here. Distress was measured by the **Kessler Psychological Distress Scale** in four studies which used versions six (K6) (Gu *et al.,* 2019; Sass *et al.,* 2017) and ten (K10) (Klompmaker *et al.,* 2019; Pinault *et al.,* 2020). This scale is a measure of non-specific psychological distress based on behavioural, emotional, cognitive, and psychophysiological manifestations (Easton *et al.,* 2017). Both versions measure the frequency with which respondents experienced symptoms in the past month, including nervousness, hopelessness, sadness, worthlessness, and fatigue (Prochaska *et al.,* 2012; Easton *et al.,* 2017). In one study data from the mental health section of the **Short Form Health Survey-36 (SF-36)** and **6-item Centre for Epidemiological Studies Depression Scale** were used to infer emotional distress (Petkus *et al.,* 2021). Subjective stress was measured by questionnaires/scales:

- In the community health survey participants rated their stress levels as 'very highly perceived', 'highly perceived', 'somewhat perceived', and 'not perceived at all' (Hwang *et al.,* 2018).
- 14-item Perceived Stress Scale (PSS)- understand to what degree respondents felt their lives were "unpredictable, uncontrollable, and overloaded" during the previous week (Mehta *et al.,* 2015). Each item was scored on a 5-point scale that ranges from "never" (0) to "very often" (4) (Mehta *et al.,* 2015).
- Short Form of the Trier Inventory for Chronic Stress rated ("Never", "Rarely", "Sometimes", "Frequently", and "Always") nine items: work overload, social overload, pressure to perform, work discontent, excessive demands from work, lack of social recognition, social tensions, social isolation, and chronic worrying (Petrowski *et al.,* 2019).

The pollutants studied were:

- Multiple pollutants in three studies: PM_{10}, $PM_{2.5}$, NO_2, black carbon, particle number counts, NO_2, O_3 and SO_4^{2-} (Mehta *et al.,* 2015; Klompmaker *et al.,* 2019; Pinault *et al.,* 2020)
- $PM_{2.5}$ in two studies (Sass *et al.,* 2017; Gu *et al.,* 2019)
- $PM_{2.5}$ and PM_{10} in one study (Petrowski *et al.,* 2019)
- $PM_{2.5}$ and NO_2 in one study (Petkus *et al.,* 2021)
- NO_2 in one study (Hwang *et al.,* 2018)

Five studies investigated how psychological distress could be affected by annual exposure to pollutants; $PM_{2.5}$ (Sass *et al.,* 2017; Gu *et al.,* 2019), including PM_{10} and NO_2 (Klompmaker *et al.,* 2019), as well as $PM_{2.5}$, NO_2, and O_3 (Pinault *et al.,* 2020) in cross-sectional studies. In addition to $PM_{2.5}$ and NO_2 in a longitudinal cohort study (Petkus *et al.,* 2021).

Higher concentrations of $PM_{2.5}$ significantly increased negative emotions particularly, nervous $\beta=0.002$ (SD 0.001) $p<0.1$, powerless $\beta=0.005$ (SD 0.001) $p<0.001$, and restless or fidgety $\beta= 0.004$ (SD 0.001) $p<0.001$ (Gu *et al.,* 2019). These results also show evidence that higher $PM_{2.5}$ concentrations could increase the likelihood of mental illnesses $\beta=0.012$ (SD 0.004) $p<0.001$ (Gu *et al.,* 2019). This association was affected by income and sex. In the high-income group $PM_{2.5}$ had no significant influence on the level of psychological disease $\beta=0.006$ (SD 0.004) compared to significant positive correlation with middle-income $\beta=0.014$ (SD 0.004) $p<0.001$ and low-income group $\beta=0.008$ (SD 0.004) $p<0.01$ (Gu *et al.,* 2019). Women $\beta=0.012$ (SD − 0.004) $p<0.01$ appeared to be slightly more sensitive than men $\beta=0.008$ (SD − 0.003) $p<0.05$ to the positive association (Gu *et al.,* 2019). All findings had small effect sizes. Similarly, another study found statistically significant associations between higher concentrations of $PM_{2.5}$ and higher psychological distress (K6 scores) before as well as after adjustment for relevant covariates (Sass *et al.,* 2017). However, adjustment attenuated the association by just over half from $\beta= 0.46$; 95% (CI: 0.35–0.56) $p<0.01$ to $\beta= 0.185$ (CI: 0.079, 0.29) $p<0.01$ (Sass *et al.,* 2017). Sociodemographic covariates accounted for the largest share of this reduction, with years of education, household income, marital/cohabitation status, and race playing the largest explanatory roles (Sass *et al.,* 2017). The addition of health behavioural and chronic disease covariates increased the magnitude of the $PM_{2.5}$ coefficient, likely due to their potential moderating effects on psychological distress (Sass *et al.,* 2017). In the stratified analysis by sex and race, a statistically significant relationship between $PM_{2.5}$ and psychological distress only remained in white women (Sass *et al.,* 2017). Using the dichotomous version of the K6 (K6 ≥13) a sizable and significant positive association for black men was found, while the significance for white women was only marginal ($p < 0.1$) (Sass *et al.,* 2017). In all pollutants studied positive significant associations were also found for increased risk of psychological distress due to previous increases in pollutant concentrations (Klompmaker *et al.,* 2019). The odds ratios for increases in pollutants were 1.03 (95% CI: 1.01-1.06) per 1.24 $\mu g/m^3$ of PM_{10}, 1.08 (95% CI: 1.06-1.11) per 0.83 $\mu g/m^3$ of $PM_{2.5}$ and 1.08 (95% CI: 1.05-1.11) per 7.85 $\mu g/m^3$ of NO_2 (Klompmaker *et al.,* 2019). When marital status, region of origin, paid occupation, household income and level of education were added, associations strongly attenuated (Klompmaker *et al.,* 2019). Neighbourhood socioeconomic status, smoking status, alcohol use and urbanization, slightly further attenuated the association (Klompmaker *et al.,* 2019). In another study, associations varied depending on the Canadian province and were affected by adjustment for individual and neighbourhood covariates (age, sex, socioeconomic position, marital status, employment status, alcohol consumption, smoking and neighbourhood marginalization) (Pinault *et al.,* 2020). In all Canadian provinces, higher $PM_{2.5}$ exposures were associated with increasing distress scores (Ontario β=0.020 $p<0.05$, Quebec β=0.021 $p<0.05$, Alberta and British Columbia β=0.021 $p<0.05$) (Pinault *et al.,* 2020). However, after adjusting for all individual and neighbourhood covariates, the positive association remained only for Quebec (β=0.009 $p<0.05$) (Pinault *et al.,* 2020). Nitrogen dioxide was positively associated with distress scores in Ontario β=0.007 ($p<0.05$) and Quebec (in unadjusted models) β=0.006 ($p < 0.05$) and adjusted model β=0.003 ($p<0.05$). However, not in Alberta and British Columbia (Pinault *et al.,* 2020). Associations between O_3 and distress were less consistent. Distress was positively associated with O_3 in both models in Quebec β=0.004 ($p < 0.05$), but negatively associated with O_3 in Ontario β=-0.002 ($p<0.05$) (unadjusted model) (Pinault *et al.,* 2020). The correlation coefficients magnitudes were very low indicating variables which have a low correlation. Petkus and colleagues demonstrated the effects of NO_2 (β= -0.025; 95% CI: -0.054-0.005) and $PM_{2.5}$ (β= -0.014; 95% CI: -0.046-0.019) on changes in emotional distress were non-significant. Higher NO_2 exposure was associated with more emotional distress at baseline (elevated by 0.056 standard deviations, per inter-quartile increment of 9.00 ppb) (Petkus *et al.,* 2021). This is equivalent to half the effect of having high blood pressure (hypertension= 0.106, 95% CI= 0.048-0.165). Although, $PM_{2.5}$ exposure was not associated with baseline emotional distress (Petkus *et al.,* 2021).

The studies by Gu and colleagues as well as Petkus and colleagues were described as moderate quality. Both studies adjusted for various health (self-rated, lifestyle factors such as smoking and alcohol use) and demographic (age, income, education level) variables. Although, the study by Petkus and colleagues was longitudinal and had a large sample, its limitations were the sample only consisted of women and how emotional distress was calculated from the two questionnaires was not explained. Gu and colleagues' data also had limitations as it did not show an average K6 score or explained what this score meant in terms of psychological distress and only one pollutant was investigated. The other studies were all described as high-quality because:

- Demographic (age, sex, household income) and health behaviours/diagnoses (alcohol consumption, current smoking, asthma, diabetes) were adjusted for.
- Defined the K6/10 score.
- Large sample sizes
- Descriptive statistics (sex and age)

Despite the adjustment variables, the potential for residual and unmeasured confounding is always a limitation in observational studies.

Subjective stress was measured in three studies (Mehta *et al.,* 2015; Hwang *et al.,* 2018; Petrowski *et al.,* 2019). The effects of annual exposure to NO_2 (Hwang *et al.,* 2018) in Korea as well as $PM_{2.5}$ and

PM_{10} in Germany (Petrowski *et al.,* 2019) were investigated in two cross-sectional studies. Generally, Hwang and colleagues found the risk of subjective stress level increased as the concentration of NO_2 increased. The OR for subjective stress was the highest among men aged 30-64 years, and this association was statistically significant (Hwang *et al.,* 2018). In the multi-pollutant model (adjusted for PM_{10}) for men aged 30-64, the ORs were elevated at the highest concentration of NO_2 (>30.08 ppb) and increased as perceived stress increased: 1.51 (1.30, 1.75) for 'I feel little stress,' 2.17 (1.83, 2.58) for 'I feel much stress,' and 2.91 (2.12, 4.01) for 'I feel stress very much' compared to 1.26 (1.04, 1.52) at 10.46-15.78 ppb (Hwang *et al.,* 2018). The same pattern was seen in women however the ORs were reduced. Respondents who said they were 'very much stressed' ORs were 1.84 (0.86, 3.94) at the highest concentration >30.08 ppb and 1.06 (0.87, 1.27) at 10.25-15.06 ppb compared to the reference (1) (Hwang *et al.,* 2018). Despite these findings, Petrowski and colleagues did not find a significant (p = 0.17/0.1) association between PM_{10} and chronic stress. However, $PM_{2.5}$ was a significant predictor of chronic stress as well as individual income and age are additional predictors (β = 8.45, p< .01, Adj.R^2= 0.03), while no other covariates were significant (Petrowski *et al.,* 2019). A one microgram per square meter (mg/m^2) increase in annual $PM_{2.5}$ exposure is associated with a 0.49 increase in one's total chronic stress level ceteris paribus (Petrowski *et al.,* 2019). This was only significant in men (Petrowski *et al.,* 2019). The addition of $PM_{2.5}$ explains 1% of the variation in chronic stress, which is less than the 2% explained by income but comparable to the 1% explained by age (Petrowski *et al.,* 2019). Income, age and $PM_{2.5}$ together explain 3% of the total variation in chronic stress (Petrowski *et al.,* 2019).

The study by Hwang and colleagues was described as moderate quality because it had a large sample (22,0435) and adjusted for health (smoking status, subjective health status, sleeping hours), meterological (temperature, precipitation) and demographic (household income, age, educational level) variables. Although, the limitations were a lack of descriptive statistics (age and sex), only one pollutant was investigated and scores from the questionnaire were not represented. Likewise, the study by Petrowski was described as moderate quality because the sample was large (746), the mean score was given from the questionaire, descriptive statistics were generated and there was adjustment for potential confounders (age, income, family status, household size, migration background, religion, education, and type of work). However, the results were difficult to understand and unclear. Furthermore, exposure at other areas such as school or work was not considered in these studies only exposure at participant's residence. Therefore, the accuracy of the exposure estimates could be lacking.

The Veterans Administration Normative Aging Cohort study conducted in Boston investigated the effects of up to a month of $PM_{2.5}$, black carbon, particle number counts, NO_2, O_3 and SO_4^{2-} exposure on the Perceived Stress Scale (PSS) (Mehta *et al.,* 2015). Statistically significant ($p<0.05$) positive associations were observed between increasing $PM_{2.5}$, black carbon, particle number counts and NO_2 at moving averages of 1, 2, and 4 weeks, and increasing stress score (Mehta *et al.,* 2015). An interquartile range increase in 1-week average pollutant exposure was associated with increase in PSS score: a 0.5-point (95% CI: 0.2-0.9) increase for 4.7 μg/m^3 of $PM_{2.5}$, a 0.5-point (95% CI: 0.1, 0.9) increase for 0.5 μg/m^3 of black carbon, and a 0.8 point (95% CI: 0.4, 1.2) increase for 0.006 ppm of NO_2 (Mehta *et al.,* 2015). Strongest associations were observed for particle number counts, a 15,997 counts/cm^3 increase was associated with 3.2-point increase in PSS score (95% CI: 2.1-4.3) (Mehta *et al.,* 2015). All moving averages of SO_4^{2-} and O_3 were not associated with PSS score (Mehta *et al.,* 2015). Observed associations were largely unaffected after excluding participant visits who reported anti-depressant medication use and after additional adjustment for smoking status as well as alcohol consumption (Mehta *et al.,* 2015). This study was described as high-quality because demographic (age, sex, paid occupation, household income, neighbourhood social economic status) and health behaviours (smoking status and alcohol consumption) were adjusted for, large study, various pollutants considered, and longitudinal data was used (1995-2007). Although, the data was limited as the sample was only made up of older males.

The information in this section is summarised in **Tables 2.21** and **2.22** below.

2.3.9.1 Summary of Stress/Distress and Pollution Associations

The associations between stress/distress and various pollutants investigated in the above section are summarised in **Table 2.21** below.

Table 2.21- Summary of the associations found between various pollutants and stress/distress.

Pollutant exposure & source	Association of the Pollutant with Stress or Distress	Reference	Key Findings	Conclusions
Short- and long-term $PM_{2.5}$	**Significant positive** association to distress	(Sass *et al.,* 2017)	Association (β=0.46) reduced after adjustment for education level, income & race (β= 0.185).	The highest number of studies (eight) found a positive association between $PM_{2.5}$ and stress or distress. In addition, only one study demonstrated no association. More research is needed which considers covariates such as deprivation to further clarify links.
		(Klompmaker *et al.,* 2019)	OR 1.08 per 0.83 μg/m³. Association reduced by socioeconomic variables.	
		(Gu *et al.,* 2019)	Only effected distress in middle (β=0.014) & low-income groups (β=0.008), not high-income. Effect sizes were small.	
		(Pinault *et al.,* 2020)	Associations were low & after adjustment for covariates the association remained in one Canadian province (β=0.009 $p<0.05$).	
	Significant positive association to stress	(Mehta *et al.,* 2015)	0.5-point increase per 4.7 μg/m³ weekly. Not affected by covariates.	
		(Petrowski *et al.,* 2019)	0.49 increase in chronic stress per mg/m² in annual exposure. Only	

			significant in men. Income & age were also predictors of stress.	
	No association to distress	(Petkus *et al.,* 2021)		
Short- and long-term PM_{10}	**Significant positive** to:			PM_{10} could be a risk factor for stress or distress. However, only four studies found a positive association and one study found a contrasting finding. However more research is needed which considers covariates.
	Stress	(Mehta *et al.,* 2015)	0.5-point increase on the scale for 4.7 μg/m³. Covariates did not affect the association.	
	Distress	(Klompmaker *et al.,* 2019)	OR 1.03 per 1.24 μg/m³. Association reduced by paid occupation, household income, education level, neighbourhood socio-economic status and urbanization.	
	No association to chronic stress	(Petrowski *et al.,* 2019)		
NO_2	**Significant positive** with stress	(Hwang *et al.,* 2018)	Increased ORs at higher concentrations (OR 2.61 >30.08 ppb, OR 1.19 at 10.46-15.78 ppb) in men.	NO_2 could be a risk factor for stress or distress however more research is needed which considers covariates.
	Significant positive association with distress	(Klompmaker *et al.,* 2019)	OR 1.08 per 7.85 μg/m³. Association reduced by socioeconomic factors.	
		(Pinault *et al.,* 2020)	Associations were lower in the adjusted model (β=0.003) and varied by Canadian province.	
		(Mehta *et al.,* 2015)	0.8-point increase on the scale for 0.006 ppm.	

	Positive association to distress	(Petkus *et al.,* 2021)	0.056 standard deviations increase per 9.00 ppb.	
O_3	**Significant positive** to distress	(Pinault *et al.,* 2020)	In one province (β=0.004). Negative association in another (β= -0.002).	The lack of research in combination with contrasting findings results in a need for further research.
	No association with stress	(Mehta *et al.,* 2015)		
Short-term SO_4^{2-}	**No association** with stress	(Mehta *et al.,* 2015)		Lack of evidence means it is difficult to come to any conclusions.
Black carbon	**Significant positive** to stress	(Mehta *et al.,* 2015)	0.5-point increase on the scale for 0.5 µg/m^3 increase	Lack of research evidence.
Particle number counts	**Significant positive** to stress	(Mehta *et al.,* 2015)	Strongest association. 3.2-point increase on the scale for 15,997 counts/cm^3	Lack of research evidence.

- $PM_{2.5}$ and NO_2 could increase psychological stress/distress levels and therefore increase the risk of mental illness.

The quality assigned to the studies in this section is summarised in **Table 2.22** below.

Table 2.22- Study quality described in the table below.

Quality	Study Citation
Moderate	(Hwang *et al.,* 2018; Gu *et al.,* 2019 Petrowski *et al.,* 2019; Petkus *et al.,* 2021)
High	(Mehta *et al.,* 2015; Sass *et al.,* 2017; Klompmaker *et al.,* 2019; Pinault *et al.,* 2020)

2.3.10 Multiple Measures of Self-reported Well-being and Mental Health

In total 10 studies used multiple measures to assess mental health and well-being. The data extraction table for these outcomes is linked here. The mental health and well-being outcomes in the ten of the studies were defined by scales/questionnaires:

- **Common mental disorders** were assessed by the Revised Clinical Interview Schedule (CIS-R) which asks about 14 symptom domains (*e.g.,* fatigue, sleep problems, irritability). **Psychotic experiences** were measured with Psychosis Screening Questionnaire (PSQ), and **somatoform disorders** were measured with the Patient Health Questionnaire subscale (PHQ-15) (Bakolis *et al.,* 2020).
- Rated **life satisfaction** out of ten using the Gallup World Poll and increase in **anxiety prevalence** from the global burden of disease (Hu *et al.,* 2021).
- Rated **life satisfaction** and the frequency of **positive/happy** including **negative/depressive emotions** (Li & Zhou, 2020).
- **Positive youth development scale** and **anxiety symptoms** by the Internalizing Disorders Scale (Ni *et al.,* 2021).
- **Perceived Stress Scale (PSS)** in addition to **Positive and Negative Affect Schedule (PANAS)** which rates positive/negative mood (Nuyts *et al.,* 2019).
- **Stress Resilience Scale**, **General Anxiety Disorder-2 questionaire**, **Rosenberg's Self-Esteem scale** (RSES), and **General Life Satisfaction questionnaire** (Petrowski *et al.,* 2021).
- **Subjective stress scale**, **quality of life** measured by EuroQol-5 dimensions (EQ-5D) index, and physician's diagnosis **suicidal ideation, or a suicide attempt** during the past year (Shin *et al.,* 2018).
- **Hospital Anxiety and Depression scale** (HADS) and Modified 4-item Perceived **Stress Scale** (Tallon *et al.,* 2017).
- **GHQ** to assess general mental health and **Symptom Checklist-90** to assess anxiety (Pelgrims *et al.,* 2021)

In one study participants were interviewed at 18 years old about previous symptoms of general psychopathology (Reuben *et al.,* 2021). Various symptoms were assessed by different tests. To summarise the symptoms measured were, **externalizing-spectrum disorder** symptoms, including alcohol, cannabis, and tobacco dependence, conduct disorder, including attention-deficit/hyperactivity disorder (Reuben *et al.,* 2021). **Four internalizing-spectrum disorder symptoms** were also measured including depression, generalized anxiety, posttraumatic stress, and eating disorders (Reuben *et al.,* 2021). **Thought disorder symptoms** were assessed via seven items about delusions and hallucinations as well as six items about unusual thoughts and feelings (prodromal symptoms: *e.g.,* “My thinking is unusual or frightening”; “People or places I know seem different”) (Reuben *et al.,* 2021). The effects of various pollutants were investigated in the studies:

- Multiple pollutants in seven studies (NO_2, NO_x, $PM_{2.5}$, PM_{10}, CO, SO_2, O_3 and black carbon) (Shin *et al.,* 2018; Bakolis *et al.,* 2020; Kim *et al.,* 202; Pelgrims *et al.,* 2021) as well as the AQI (Li & Zhou, 2020; Ni *et al.,* 2021)
- NO_2 in one (Nuyts *et al.,* 2019)
- PM_{10} in one (Petrowski *et al.,* 2021)
- $PM_{2.5}$ in one study (Hu *et al.,* 2021)
- $PM_{2.5}$ and NO_2 in one (Tallon *et al.,* 2017)
- NO_x (NO_2 and NO) and $PM_{2.5}$ in one study (Reuben *et al.,* 2021)

Six studies investigated the effects of annual exposure to pollutants with a cross-sectional design (Shin *et al.,* 2018; Li & Zhou, 2020; Petrowski *et al.,* 2021) and repeated cross-sectional design (Ni *et al.,* 2021; Bakolis *et al.,* 2020; Pelgrims *et al.,* 2021). In Korea, significant positive associations were generally found between increasing concentrations of PM_{10}, NO_2, and CO and subjective stress, poor quality of life, as well as suicidal ideation (Shin *et al.,* 2018). However, not suicide attempts. The ORs for the highest quartile of NO_2 were ~1.2 for subjective stress, ~1.58 for poor quality of life, and ~1.39 for suicidal ideation (Shin *et al.,* 2018). The ORs for the highest quartile of PM_{10} were ~1.18 for subjective stress, ~ 1.25 for poor quality of life, and ~1.25 for suicidal ideation (Shin *et al.,* 2018). The ORs for the highest quartile of CO were ~ 1.1 for subjective stress, ~ 1.19 for poor quality of life, and ~ 1.22 for suicidal ideation (Shin *et al.,* 2018). The clearest dose-response relationship was found for NO_2 and all mental health outcomes. However, no association was found between SO_2 and all mental health outcomes since all the 95% CIs went through 1 (Shin *et al.,* 2018). In terms of sex differences, men had increased prevalence of subjective stress with exposure to PM_{10} and prevalence of poor quality of life with exposure to CO compared with women (Shin *et al.,* 2018). The risk of suicidal ideation had no difference according to sex ($p > 0.05$). In subjects <65 years old, high quartiles of PM_{10}, NO_2, CO and SO_2 had a higher risk of poor quality of life than subjects >65. In Chinese cities, reduced air quality also significantly reduced well-being (coefficient -0.01 $p<0.001$); specifically, life satisfaction (coefficient −0.01 $p<0.001$) and happiness frequency (coefficient −0.01 $p<0.001$) (Li & Zhou, 2020). Similarly, in a study conducted in Germany, a microgram per cubic meter ($\mu g/m^3$) increase in annual PM_{10} exposure was significantly associated with a decrease of 0.34 in subjective life satisfaction score ($p < 0.001$), 0.08 in self-esteem ($p = 0.011$) and 0.15 stress resilience ($p < 0.001$) ceteris paribus (Petrowski *et al.,* 2021). However, there was no significant association with anxiety symptoms (coefficient= 0.006, $p = 0.181$) (Petrowski *et al.,* 2021). Age and income were significant predictors in all models except age for self-esteem ($p = 0.177$). These associations varied in females and males. In females' only life satisfaction and self-esteem were negatively impacted by $PM_{10,}$ but this was only significant for self-esteem (-0.10, p=0.22) (Petrowski *et al.,* 2021). Although, a μg/m^3 increase in PM_{10} was associated with a 0.15 (males) or 0.13 (females) decrease in subjective stress resilience score ceteris paribus (Petrowski *et al.,* 2021). All the studies above were described as moderate quality:

- All large studies
- Most described participants in terms of age and sex apart from Li & Zhou (2020).
- Multiple pollutants were investigated in most studies apart from Petrowski *et al*. (2019)
- Mental health was defined by a simple scale (Li & Zhou, 2020), clearly defined questionnaires for each outcome (Petrowski *et al.,* 202), and a simple scale to measure stress, EQ-5D index and suicide ideation or attempt was not defined (Shin *et al.,* 2021).
- In terms of adjustment variables; age and income (Petrowski *et al.,* 2019), demographic variables (sex, marital status, age, education, income) (Li & Zhou, 2020) and demographic variables (age, sex, education, income, residence) as well as lifetsyle factors (smoking, alcohol consumption, physical activity, medical history) (Shin *et al.,* 2018).

A repeated cross-sectional study in Brussels found no significant associations between 1 μg/m^3 increases in $PM_{2.5}$, PM_{10}, black carbon, O_3, NO_2 and general mental health (GHQ-4 score) or anxiety disorders (Pelgrims *et al.,* 2021). For example, the ORs per 1 μg/m^3 increase in black carbon for general mental health and anxiety respectively were, 1.00 (0.76–1.33) and 1.07 (0.79–1.45). All associations per 1 μg/m^3 were close to one. No significant interactions were found between pollutants and sex or age (Pelgrims *et al.,* 2021). In a Chinese city worse air quality was found to have a negative effect on anxiety and positive youth development in children (average age 12.46) (Ni *et al.,* 2021). As air quality decreased the positive youth development score also decreased −0.017 (t-value = −4.94 p=0.01) (Ni *et al.,* 2021). Similar associations exist for the four sub-dimensions of the positive youth development scale: cognitive behavioural competence (-0.016 p<0.001), prosocial attributes (-0.007 p<0.10), positive and healthy identity (-0.009, p<0.05), and general positive youth development qualities (-0.016, p<0.001) (Ni *et al.,* 2021). Worse air quality also had a slight negative effect on anxiety symptoms. The regression coefficients of the air pollution index on the total internalizing disorders (0.118, p<0.10), anxiety (0.042, p<0.05), neuroticism (0.027, non-significant), and withdrawal behaviours (0.021, p<0.05) (Ni *et al.,* 2021). The study by Bakolis *et al*. (2020) in London showed ORs for the air pollutants and common mental in addition to somatoform disorders in the adjusted model respectively were significantly positive:

- NO_2 1.39 (1.05-1.85) (p<0.005) and 1.30 (1.02-1.64) (p<0.005)

- NO_x 1.37 (1.04-1.81) ($p<0.005$) and 1.28 (1.02-1.61) ($p<0.005$)
- $PM_{2.5}$ 1.18 (1.02-1.37) ($p<0.005$) and OR 1.19 (1.04-1.35) ($p<0.01$)

Adjustment for age, sex, socioeconomic status, smoking status, ethnicity, frequency of drinking, physical activity, and noise made no significant difference and barely attenuated the association (Bakolis *et al.,* 2020). Positive associations were found between PM_{10} and mental disorders in addition to somatoform disorders, but these associations were non-significant OR 1.19 (0.97-1.45) and 1.10 (0.93-1.30) (Bakolis *et al.,* 2020). In contrast, negative associations were observed for O_3 and mental disorders in addition to somatoform disorders respectively OR 0.78 (0.60-1.02) and 0.86 (0.7-1.07) (Bakolis *et al.,* 2020). These associations were more pronounced in non-movers with common mental disorders for NO_2 and NO_x (Bakolis *et al.,* 2020). From the first survey, psychotic experiences were extracted and appeared to have an association with PM_{10} [OR of 1.33 (95% CI 1.14-1.55)]. However, estimates were attenuated when co-exposure models were employed due to issues of high multicollinearity.

The studies by Bakolis *et al*. (2020) and Pelgrims *et al*. (2021) were reported as high quality because both had large sample sizes (>1000), described participants in terms of age and sex and investigated multiple pollutants. Moreover, both studies adjusted for lifestyle as well as demographic variables (*e.g.,* age, sex, socioeconomic status, physical activity). The study by Ni and colleagues was also large (>1000), investigated overall air quality and adjusted for confounders (sex, place of growth, only child or not, migrant, or local resident status, parents' educational levels, household income, and family intactness). However, parents' mental health was not considered and the scores from the questionaire were not explained in terms of those who were more anxious or had more negative development. Therefore, the study was described as moderate quality.

Three cohort studies investigated long-term exposure, annual (Hu *et al.,* 2021; Reuben *et al.,* 2021) and 1-7 years (Tallon *et al.,* 2017). In 51 countries with annual $PM_{2.5}$ exposure higher than 10 µg/m^3 the negative effects on life satisfaction and anxiety were significant when unemployment, social support, generosity, positive and negative emotions were included (Hu *et al.,* 2021). However, when income was added to the regression the results became insignificant (Hu *et al.,* 2021). For example, the association between $PM_{2.5}$ and life satisfaction changed from significant −0.413 $p<0.01$ (0.115) to insignificant −0.128 (0.097) (Hu *et al.,* 2021). In addition, the association between $PM_{2.5}$ and anxiety changed from significant 0.0000465 $p<0.01$ (0.0000159) to insignificant 0.0000206 (0.0000165) (Hu *et al.,* 2021). This could be because income level had a significant correlation with happiness [0.521 $p<0.01$ (0.0643)] (Hu *et al.,* 2021). In the high-income group, $PM_{2.5}$ was negatively correlated with life satisfaction (−0.439) which was significant whereas no significant association was found for anxiety. In the low-income countries, a positive significant correlation was demonstrated between $PM_{2.5}$ and anxiety (0.000047, $p<0.05/0.10$) whereas the effect on life satisfaction was non-significant (Hu *et al.,* 2021). In another study, exposure to NO_2 in those living in the US aged 57-84 was found to increase stress [0.11 (95% CI: 0.02-0.19)] (Tallon *et al.,* 2017). However, NO_2 exposure was not found to effect anxiety [0.05 (-0.06, 0.17)] (Tallon *et al.,* 2017). In addition, $PM_{2.5}$ did not influence anxiety [0.02 (−0.21, 0.25)] or stress [− 0.04 (− 0.21, 0.14)] (Tallon *et al.,* 2017).

A traditional longitudinal, population-based twin cohort study in the UK investigated past-year symptoms of mental disorders and annual air pollutant exposure in adolescents (Reuben *et al.,* 2021). All associations were adjusted for sex, family socioeconomic status, family psychiatric history, participant history of emotional and behavioural problems, and tobacco smoking (Reuben *et al.,* 2021). Each interquartile range increment increase in NO_x exposure was associated with a 1.40-point increase in general psychopathology (95% CI, 0.41-2.38; $p= 0.005$) (Reuben *et al.,* 2021). Individuals in the highest quartile of NO_x (38.75-113.07 $\mu g/m^3$) scored 2.62 points higher on general psychopathology than their peers in the bottom 3 quartiles (95% CI, 0.96-4.27; $p= 0.002$) (Reuben *et al.,* 2021). NO_x exposure was associated with all psychiatric domains. For children exposed to the highest levels of continuously measured NO_x associations were weakest ($\beta= 1.81$; 95% CI, 0.16-3.45; $p =0.03$) for internalizing symptoms; medium ($\beta= 2.37$; 95% CI, 0.81-3.94; $p= 0.003$) for externalizing symptoms; and strongest ($\beta= 3.18$; 95% CI, 1.46-4.90: $p<0.001$) for thought disorder symptoms. Whereas exposure to continuously measured $PM_{2.5}$ was not associated with general psychopathology ($\beta= 0.45$; 95% CI, −0.26 to 1.15; $p= 0.22$). However, participants in the highest quartile of $PM_{2.5}$ exposure scored 2.04 points higher on general psychopathology (95% CI, 0.36-3.72; $p= 0.02$) than their peers in the bottom 3 quartiles. In addition, associations were significant for thought disorder symptoms ($\beta= 2.50$; 95% CI, 0.75-4.25; $p= 0.005$) when pollutant extremes were considered (Reuben *et al.,* 2021). The co-pollutant models implicated NO_x alone in these significant findings; strength of the association for NO_x with general psychopathology was barely attenuated ($\beta= 2.54$ vs original $\beta= 2.62$, 3% attenuation), whereas for $PM_{2.5}$ the association was fully attenuated ($\beta= 0.10$ vs original $\beta= 2.04$, 95% attenuation) (Reuben *et al.,* 2021). Despite, findings NO_x was higher in neighbourhoods with worse physical, social, and economic conditions (Pearson r's between 0.25 and 0.45) adjustment for deprivation, dilapidation, disconnection, and dangerousness did not change the results.

The study by Hu and colleagues was described as moderate quality because one pollutant was measured and no information on sex, age or the countries participants lived in was given. In comparison, the study by Tallon and colleagues was described as high quality since multiple pollutants were studied and age as well as sex of participants was described. In terms of adjustment variables, Hu and colleagues included unemployment, social support, generosity, income level, positive and negative emotions. Whereas Talon and colleagues included meterological variables (wind speed, temperature, total precipitation) in the pollution model as well as demographic and lifestyle factors (gender, age, race/ethnicity, education, season, smoking, region, median household income of census tract). Similarly, Reuben and colleagues' study was described as high quality because it had detailed methodology, investigated co-exposure, a large sample and adjusted for covariates that could affect the adolescents' mental health (family socioeconomic status, family psychiatric history, participant history of emotional and behavioural problems in early childhood and tobacco smoking).

A panel study in a city in Belgium was the only study to investigate short-term exposure (five days before the questionnaires were answered) to NO_2 in retired couples (aged 58-76) (Nuyts *et al.,* 2019). An increase of 10 μg/m^3 in NO_2 concentration was significantly associated with a decrease of 1.3 points in the positive affect (95% CI -2.49 to −0.17) and an increase of 0.11 points in the negative affect (95% CI 0.02 to 0.20) (Nuyts *et al.,* 2019). The association with decreased positive affect was stronger when physical activity was below median value of 9,362 steps per day (β = −2.68; CI: 4.87 to −0.49, *p*-value= 0.08) (Nuyts *et al.,* 2019). However, no statistically significant associations were observed with perceived stress [3% (−14%-24%)] (Nuyts *et al.,* 2019). This study was described as low to moderate quality because the sample size was small (20), one pollutant was measured and one individual in the couple wore the clip-on sampler with unknown reliability (Lewis and Edwards, 2016). However, numerous measurements of NO_2 and well-being were taken over the year. In addition to adjustment for age, sex, temperature, number of steps and duration of sunlight.

The information in this section is summarised in **Tables 2.23** and **2.24** below.

2.3.10.1 Summary of Multiple Self-reported Mental Health and Pollution Associations

The associations between multiple measures of self-reported mental health/well-being and various pollutants investigated in the above section are summarised in **Table 2.23** below.

Table 2.23- Summary of the associations found between various pollutants and multiple measures of self-reported mental health/well-being.

Pollutant exposure & source	Association of the Pollutant with Self-reported Mental Health	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Significant positive** with common mental & somatoform disorders	(Bakolis *et al.,* 2020)	Respectively ORs 1.18 & 1.19. Not effected by socio-economic status, age, sex & ethnicity.	There was a lot of variation found in terms of the links, covariables, mental health outcomes, and participants. This resulted in difficulties coming to any conclusions.
	Reduced life satisfaction & **increased** anxiety	(Hu *et al.,* 2021)	Higher than 10 µg/m³. Became in-significant when income was added & associations varied by income level.	
	No association to:			
	General mental health & anxiety disorders	(Pelgrims *et al.,* 2021)	No significant effect by age or sex.	
	Anxiety or stress	(Tallon *et al.,* 2017)	Respectively 0.02 or − 0.04 in 57–84-year-olds.	
	General psychopathology.	(Reuben *et al.,* 2021)	Coefficient= 0.45. But participants in the highest quartile scored 2.04 points higher than in lower quartiles.	

PM_{10}	**Significant** to **reduced** life satisfaction, self-esteem & stress resilience	(Petrowski *et al.,* 2021)	Respective values 0.34 ($p < 0.001$), 0.08 ($p = 0.011$) & 0.15 ($p < 0.001$) per µg/m^3. Income was a significant predictor for all models. Men at higher risk of reduced stress resilience.	Similar, to the conclusion above. Since, PM_{10} had a negative effect on some mental health outcomes, but some studies also found no association. These differences could be caused by the type of mental health issue. However, this would require more research to confirm.
	Significant positive with:			
	Stress & poor quality of life	(Shin *et al.,* 2018).	Significantly increased the risk of stress in men & poor quality of life <65 compared to women & >65.	
	Psychotic disorders	(Bakolis *et al.,* 2020)	OR 1.33. Not affected by covariates stated previously.	
	Positive to common mental & somatoform disorders	(Bakolis *et al.,* 2020)	Respectively OR 1.19 & 1.10. Non-significant.	
	No association to:			
	General mental health & anxiety disorders	(Pelgrims *et al.,* 2021)	No significant effect by age or sex.	
	Anxiety symptoms	(Petrowski *et al.,* 2021)	Coefficient= 0.006, p= 0.181.	
	Suicidal attempts	(Shin *et al.,* 2018)	95% CI went through 1.	

NO_2	**Significant positive** with:			Associations varied in terms of the mental health outcome investigated. Although NO_2 was found to negatively impact in slightly more studies. Therefore, it is vital more research is carried out.
	Common mental & somatoform disorders	(Bakolis *et al.,* 2020)	Strongest OR 1.39. Not affected by confounders.	
	Stress, poor quality of life & suicide ideation	(Shin *et al.,* 2018)	ORs ~1.2, ~1.58 & ~1.39. Clearest dose-response relationship (PM_{10} & CO). Significant poor quality of life <65.	
	Negative affect.	(Nuyts *et al.,* 2019)	0.11 points increase. Strengthened by reduced activity.	
	Positive association to:			
	Increased stress	(Tallon *et al.,* 2017)	By 0.11 in 57–84-year-olds.	
	No association to			
	General mental health & anxiety disorders	(Pelgrims *et al.,* 2021)	No significant effect by age or sex.	
	Anxiety	(Tallon *et al.,* 2017)	Coefficient= 0.05 in 57–84-year-olds.	
	Stress	(Nuyts *et al.,* 2019).	3% (−14%-24%) in 58–76-year-olds.	
	Suicidal attempts	(Shin *et al.,* 2018)	95% CI went through 1.	
NO_x	**Significant positive** to:			Two studies showed NO_x decreased mental health and the association appeared not to be affected by
	Common mental & somatoform disorders	(Bakolis *et al.,* 2020)	Second strongest association (1.37). Not affected by covariates.	

	General psychopathology	(Reuben *et al.,* 2021)	1.40-point increase. Co-exposure with $PM_{2.5}$ showed NO_x strength was barely reduced. Higher concentrations (38.75-113.07 μg/m^3) had more negative effects. Not affected by covariates.	covariates. More high-quality studies investigating the effects of NO_x on mental health is necessary.
O_3	**No association** to: mental health & anxiety disorders	(Pelgrims *et al.,* 2021)	No significant effect by age or sex.	O_3 does not appear to have a negative effect on mental health however only two studies found this so more research is needed.
	Negative association to common mental & somatoform disorders	(Bakolis *et al.,* 2020)	ORs 0.78 (0.60-1.02) and 0.86 (0.7-1.07) respectively.	
SO_2	**No association** to stress, poor quality of life & suicidal ideation.	(Shin *et al.,* 2018)	95% CI went through 1.	Lacks evidence so further research is required to clarify any potential effects.
CO	**Significant positive** to:			Associations varied depending on the mental health issue investigated in both studies. This in combination with the lack of research means it is difficult to come to any conclusions.
	Stress, suicidal ideation & poor quality of life	(Shin *et al.,* 2018)	Significantly increased risk of poor quality of life in men and < 65.	
	No association to suicide attempts	(Shin *et al.,* 2018)	95% CI went through 1.	
Black carbon	**No association** to general mental health & anxiety disorders	(Pelgrims *et al.,* 2021)	No significant effect by age or sex.	Only one study therefore more

				evidence is needed to come to conclusions.
Reduced air quality	**Increased anxiety** symptoms & **reduced** positive youth development.	(Ni *et al.,* 2021)	Respectively 0.042 & −0.017 in children (average age 12.46).	Reduced air quality appears to negatively affect well-being in children and adults. Although, more research is needed to confirm this.
	Significantly reduced well-being	(Li & Zhou, 2020)	Well-being, life satisfaction & happiness (-0.01)	

- Overall due to the heterogeneity of the methods, mental health outcomes and pollutants it is difficult to come to any conclusions.

The quality assigned to the studies in this section is summarised in **Table 2.24** below.

Table 2.24- Study quality described in the table below.

Quality	**Study Citation**
Low/moderate	(Nuyts *et al.,* 2019)
Moderate	(Shin *et al.,* 2018; Li & Zhou, 2020; Hu *et al.,* 2021; Ni *et al.,* 2021; Petrowski *et al.,* 2021)
High	(Tallon *et al.,* 2017; Bakolis *et al.,* 2020; Pelgrims *et al.,* 2021; Reuben *et al.,* 2021)

2.3.11 Contact with Mental Health Professionals for Multiple Psychiatric Disorders

In total 18 studies had an outcome of contact with mental health professionals for multiple mental disorders. Contact was at participants homes or hospital admissions during inpatient, outpatient, and emergency department visits. The data extraction table for these outcomes is linked here. Outpatient visits are when patients attend a hospital for treatment without staying overnight (NHS, 2023a). Whereas inpatient care is when a patient lives in hospital while under treatment (NHS, 2023a). Emergency department is a medical treatment facility specialising in emergency medicine, the acute care of patients who present without prior appointment, either by their own means or by an ambulance. Contact with mental health professionals was defined in the studies by:

- **Emergency department visits** (Oudin *et al.,* 2018; Bernardini *et al.,* 2019)
- **Outpatient visits** (Lowe *et al.,* 2020; Lu *et al.,* 2020)
- **Emergency ambulance dispatches** (Liu *et al.,* 2019)
- **ICD-10 diagnoses** in different circumstances in ten studies:
    - **Emergency department visits** in four studies (Brokamp *et al.,* 2019; Kim *et al.,* 2019; Szyszkowicz *et al.,* 2020; Muhsin *et al.,* 2021),
    - **Outpatient visits** in one study (Li *et al.,* 2020),
    - **Hospital admissions** in three studies (Chen *et al.,* 2018b; Qui *et al.,* 2019; Wu *et al.,* 2020)
    - **Anxiety emergency department visits** and **suicides** from the national statistics institute (Diaz *et al.,* 2020)
    - **Inpatient, home treatment team** and **Community mental health services** (CMHS) (Newbury *et al.,* 2021)
- **ICD-9-CM** diagnoses in **emergency department visits** in two studies (Thilakaratne *et al.,* 2020; Nguyen *et al.,* 2021)
- **Multiple ways** in one study (Khan *et al.,* 2019). Data on bipolar, schizophrenia and personality disorders were collected from US inpatient, outpatient, medical procedures, and prescription medication records. These conditions were diagnosed with ICD-9-CM. In Denmark, ICD8/10 inpatient, outpatient, and emergency department records for these disorders were used.

The pollutants investigated in the studies were:

- Mainly multiple pollutants in different combinations PM_{10}, $PM_{2.5}$, O_3, NO_2, CO, and SO_2 (Chen *et al.,* 2018b; Bernardini *et al.,* 2019; Khan *et al.,* 2019; Kim *et al.,* 2019; Qui *et al.,* 2019; Diaz *et al.,* 2020; Li *et al.,* 2020; Lu *et al.,* 2020; Newbury *et al.,* 2021; Oudin *et al.,* 2018; Szyszkowicz *et al.,* 2020)
- $PM_{2.5}$ (Brokamp *et al.,* 2019; Liu *et al.,* 2019)

- $PM_{2.5}$ and PM_{10} (Lowe *et al.,* 2021; Wu *et al.,* 2020; Muhsin *et al.,* 2021)
- $PM_{2.5}$ and O_3 (Nguyen *et al.,* 2021)
- CO and NO_2 (Thilakaratne *et al.,* 2020)

2.3.11.1 Emergency Services

Overall, ten studies had an outcome of emergency services. Eight studies had an outcome of emergency department visits for multiple psychiatric disorders (Oudin *et al.,* 2018; Bernardini *et al.,* 2019; Brokamp *et al.,* 2019; Kim *et al.,* 2019; Szyszkowicz *et al.,* 2020; Thilakaratne *et al.,* 2020; Muhsin *et al.,* 2021; Nguyen *et al.,* 2021). One study only investigated anxiety emergency department visits and suicides (Diaz *et al.,* 2020). Another study had an outcome of emergency ambulance dispatches (Liu *et al.,* 2019). Daily air pollutant exposure was investigated in five time-series studies (Bernardini *et al.,* 2019; Liu *et al.,* 2019; Diaz *et al.,* 2020; Thilakaratne *et al.,* 2020; Nguyen *et al.,* 2021), four time-stratified case-crossover studies (Oudin *et al.,* 2018; Brokamp *et al.,* 2019; Szyszkowicz *et al.,* 2020; Muhsin *et al.,* 2021) and one cross-sectional study (Kim *et al.,* 2019).

In a town and city in Italy, the number of daily emergency service admissions was positively correlated with O_3 (regression coefficient= 0.013, SE 0.005) ($p<0.001$) (Bernardini *et al.,* 2019). Virtually all correlations were statistically significant at the 1% level for $O_{3,}$ and adjustment for other pollutants had no effect (Bernardini *et al.,* 2019). Whereas negative correlations were found with daily concentrations of PM_{10} -0.005 SE [0.004], $PM_{2.5}$ -0.009 SE [0.007], NO_2 -0.0010 SE [0.009], CO -0.690 [0.345] ($p<0.1$) and emergency visits in the univariant regression (Bernardini *et al.,* 2019). A study conducted in Madrid, found no association between the pollutants (PM_{10}, $PM_{2.5}$, NO_2, O_3) and anxiety emergency department visits as well as suicide (Diaz *et al.,* 2020). The relative risks for the association were not provided. Similarly, a time-series analysis in California found CO and NO_2 were non-significantly associated with all mental disorders, bipolar disorder, schizophrenia, substance abuse, nor suicide/self-harm (Thilakaratne *et al.,* 2020). An increase in CO (0.28 ppm) corresponded to a change in risk of −0.21% (95% CI −0.90, 0.49) for all mental disorders, 0.16% (−1.41, 1.75) for bipolar, 0.64% (−1.48, 2.82) for schizophrenia, 0.75% (−0.27, 1.78) substance abuse and −1.18 (−3.38, 1.06) suicide/self-harm (Thilakaratne *et al.,* 2020). An increase in NO_2 (10.79 ppm) corresponded to a change in risk −0.34% (95% CI −1.27, 0.61) for all mental disorders, −0.26 (−2.14, 1.65) for bipolar, 0.45% (−1.40, 2.32) for schizophrenia, -0.09% (−1.25, 1.07) substance abuse and -0.10% (−2.70, 2.58) suicide/self-harm. These associations varied by season. Increases in NO_2 were associated with reduced risk of suicide/self-harm (−4.21%, 95% CI: −6.94, −1.39%) during the cool season and substance abuse (change in risk: −2.14%, 95% CI: −3.80, −0.46%) in the warm season. Additionally, CO was associated with a reduced change in risk of all mental disorders (−1.77%, 95% CI: −2.40, −1.13%), and suicide/self-harm visits (−3.36%, 95% CI: −5.56, −1.12%) in the cool season (Thilakaratne *et al.,* 2020).

Contrastingly, another study conducted in California found O_3 and $PM_{2.5}$ increased the risk of mental health emergency department visits (Nguyen *et al.,* 2021). Significant positive associations were found between cumulative 7-day exposure per 10 ppb of O_3 and all mental health (0.64%, 95%CI: 0.21-1.07), self-harm/suicide (1.43%, 95%CI: 0.35-2.51), mood/affective disorders (1.52%, 95% 0.69, 2.36) including bipolar (2.83%, 95% CI: 1.53, 4.15). Additionally, significant positive associations were found between 30-day lag exposure to O_3 and increased risk of neurotic disorders (1.22%, 95% CI: 0.48-1.97). Same day mean 10 μg/m^3 increases in $PM_{2.5}$ were significantly positively associated with 0.42% (95%CI: 0.14-0.70) increase in all mental health and 0.57% (95%CI: 0.22-0.92) increase in neurotic disorders (Nguyen *et al.,* 2021). Schizotypal/delusional, schizophrenia, psychosis and substance use were not statistically significant for O_3 or $PM_{2.5}$ and positive or negative associations varied depending on the lag (Nguyen *et al.,* 2021). Nguyen and colleagues found risk varied by age group and was generally greater for females and in the warm season (May to October). Change in risk was significantly elevated for O_3 exposure in children (aged 0-18) for all mental health, psychosis, neurotic, substance abuse, self-harm/suicide, and bipolar compared to adults (aged 19-65+). The highest risk categories for the 0-to-18 age group were visits related to psychosis (12.71%, 95% CI: 8.82, 16.73) and bipolar disorder (11.56%, 95% CI: 7.39, 15.90). Contrastingly, $PM_{2.5}$ significantly increased mental health risk for the 65+ age group for all mental health, neurotic/stress, and schizotypal/delusional disorders. Following O_3 exposure, females had a significantly increased risk of substance use disorder [1.77%, 95% CI: 0.60, 2.96] compared to males (-0.01%, 95% CI: -1.20, 1.19 [P_{diff} = 0.04]). Significantly increased risk was found in the warm compared to cold season for $PM_{2.5}$ exposure in all mental health, psychosis, neurotic/stress, mood/affective disorders, bipolar, self-harm/suicide, schizotypal/delusional, and schizophrenia.

In Beijing, significant positive associations were found between 10 μg/m^3 increases in $PM_{2.5}$ on the same day (lag 0), lag 1, lag 2, lag0-2 and psychiatric emergencies (Liu *et al.,* 2019). The highest percentage changes were found at lag0 for non-suicide related emergencies (0.22% [95%CI: 0.10–0.34%], p<0.001) and overall emergency ambulance dispatches (0.12% [95% CI, 0.03–0.22%], p= 0.013). In addition to suicide related emergencies at lag 2 (0.12% [95%CI: 0.01–0.24%], p= 0.041). After adjustment for sunlight duration, the associations remained significant, while the cumulative effects (lag 0-2) disappeared. An age effect was observed where children (aged <18) showed a higher risk of suicide-related emergencies after $PM_{2.5}$ exposure compared to adults (18≤ age ≤64) (−0.36% vs.

−0.04% at lag 3, p= 0.037). The elderly (≥65) showed a lower risk of non-suicide related emergencies compared to 18–64-year-olds (−0.36% vs. −0.04% at lag 3, p= 0.037). There was no evidence of effect modification by sex and season based on the results of stratified analysis.

All these time-series studies were described as moderate quality predominantly because individual-level characteristics related to socioeconomic status, medical history, medication use, and/or access to mental health care were not included. These variables, among others, are possible moderators influencing the relationship between air pollutants and mental health (Bhaskaran *et al.,* 2013). Diaz and colleagues did not report the values from the association between mental health and chemical pollutants which are important to see even if no association was found. However, the effects of the temperature and noise were investigated as well as multiple chemical pollutants in this study.

A case-crossover study in Sweden showed same day exposure to a 10 μg/m^3 increase in PM_{10} significantly increased the number of emergencies by 2.3% (95% CI 0.4–4.3%) (Oudin *et al.,* 2018). However, no association was found for NO_2 (0.3% (95% CI −0.8–1.5) or O_3 (0.1% (95% CI −0.6–0.9) (Oudin *et al.,* 2018). In the three pollutant (PM_{10}, NO_2, O_3) model the increase was 1.4% (95%CI -0.8–3.7) at lag 0 however at lag 1 to lag 7 associations were generally lower and not statistically significant (Oudin *et al.,* 2018). In the warmer season (April to September) visits increased with increasing PM_{10} in both single-pollutant and two-pollutant models. For example, an increase of 3.6% (95% CI, 0.4–7.0%) was observed with a 10 μg/m^3 increase in PM_{10} adjusted for NO_2 compared to 0.5% (95%CI −2.5-3.5%) in the cold season. In the three-pollutant models the increase was 3.3% (95% CI, −0.2-6.9) but this was non-significant. There were no clear associations between the outcome and NO_2, O_3, or PM_{10} during the colder season (October to March) (Oudin *et al.,* 2018). Another study in Sweden found, in adults emergency department visits were statistically significantly associated with both PM_{10} and $PM_{2.5}$ (Muhsin *et al.,* 2021). The RR was 1.016 (95% CI 1.004–1.028) per 10 μg/m^3 increase in PM_{10} at lag 0 (the same day) (Muhsin *et al.,* 2021). Similarly, the RR was 1.020 (95%CI 1.003–1.038) per 10 μg/m^3 increase in $PM_{2.5}$ over lags 0–2 for psychiatric emergencies (Muhsin *et al.,* 2021). However, no association was found for specific diagnostic groups (depression, anxiety, and substance abuse). In females, emergencies were increased at lag 0 and lag 1, and in males at lag 1 and lag 2. In the age-stratified analysis, emergencies significantly increased following PM exposure amongst individuals aged 35–65 years old at lag 0–2. Patients with ongoing psychiatric contact had significant associations on earlier lags (lags 0 and lag 1) and increased risk of psychiatric emergencies compared to those with no ongoing contact (Muhsin *et al.,* 2021). In Ohio, Brokamp and colleagues investigated the effects of $PM_{2.5}$ on children (<18). Positive significant associations were found between 10 μg/m^3 increases in

$PM_{2.5}$ and any psychiatric emergency department visit 1 day OR 1.07 (95% CI: 1.02-1.12) and 2 days later OR 1.05 (95% CI: 1.00-1.10). The ORs were for schizophrenia on the same day 1.25 (95%CI: 1.00-1.57), adjustment disorder 1 day later 1.24 (95%CI: 1.02-1.52) and 2 days later 1.24 (95% CI: 1.02-1.51), other mood disorders 2 days later 1.15 (95%CI: 1.02-1.30), as well as suicidality 1 day later 1.44 (95%CI: 1.03-2.02) (Brokamp *et al.,* 2019). When considering deprivation, associations between a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and emergency visits were stronger for children living in high-versus low-deprivation communities for anxiety on the same day (OR 1.39, 95%CI: 0.9-2.00) vs. (0.77 95%CI: 0.57-1.05) and 1 day later (OR 1.39, 95%CI: 0.96-2.01) vs. (0.85, 0.62-1.17), and suicidality related visits on the same day (OR 1.98 95% CI: 1.22-3.23) vs. 0.93 (0.60-1.45) (Brokamp *et al.,* 2019). Conversely, associations with adjustment disorder were weaker for children living in high- versus low-deprivation areas, for visits on the same day OR 0.82 (95% CI: 0.62-1.08) vs. 1.25 (95% CI: 0.96-1.62)] and 1 day later OR 1.00 (95% CI: 0.76-1.33) vs. 1.50 (95% CI: 1.16-1.93) (Brokamp *et al.,* 2019). Another study explored the effects of pollutants (NO_2, O_3, $PM_{2.5}$) on children as well as young adults (8-24 years old) in Toronto (Szyszkowicz *et al.,* 2020). Same day $PM_{2.5}$ increases (6.03 $\mu g/m^3$ [IQR]) were significantly positively associated to all (RR 1.01 95% CI: [1.00–1.02]) and female patients (RR 1.02 [1.00–1.03]). One-day lagged exposure was also significantly positively associated with emergency department visits for $PM_{2.5}$ (RR 1.02 (1.01–1.03)) in all participants, for NO_2 (IQR = 9.1 ppb, RR 1.02 (1.00–1.04)), and O_3 (IQR = 16.0 ppb, RR 1.06 (1.01–1.10)) in males aged 13-18 (Szyszkowicz *et al.,* 2020).

The time stratified case cross-over design of these studies controls for time (day, month, and year), temperature and short-term time invariant potential confounders (age, sex, socioeconomic status) which makes these moderate to high quality studies (Peters *et al.,* 2006). However, the studies varied in different ways. Oudin and colleagues' study was described as moderate quality because there was no information on age, sex, or diagnosis (only emergency department visits) or cause for visits. Although multiple pollutants were investigated. Despite, Brokamp and colleagues only investigating the effects of $PM_{2.5}$, how mental health was diagnosed was clear and information was given on sex and age of participants. In the studies by Szyszkowicz and colleagues as well as Muhsin and colleagues it was clear how mental illness was diagnosed (ICD-10), large sample sizes and multiple pollutants were investigated. Szyszkowicz *et al*. (2020) had information on the age and sex of participants but only explored overall psychiatric disorders whereas Muhsin *et al*. (2021) explored individual types too. However, both studies used fixed site monitors so individual exposure would be difficult to measure accurately. Therefore, these studies were described as moderate to high.

A cross-sectional study of adolescents' and adults (>15) in Korea, found only increases in NO_2 and O_3 affected psychiatric emergency department visits (Kim *et al.,* 2019). Neurotic, stress-related and somatoform disorders were significantly increased on lag day 1 by NO_2 (RR 1.015, 95%CI 1.001–1.031) (Kim *et al.,* 2019). Ozone was associated with an increase in schizophrenia, schizotypal and delusional disorders (RR 1.039, 95%CI 1.001–1.079) (Kim *et al.,* 2019). Whereas CO was significantly associated with a decrease in these disorders (RR 0.966, 95%CI 0.944–0.989). Additionally, SO_2 was significantly associated with decreased emergency department visits for all psychiatric diseases on lag day 1 (RR 0.991, 95%CI 0.982–0.999) (Kim *et al.,* 2019). Daily emergency department visits were not associated with $PM_{2.5}$ (Kim *et al.,* 2019). However, in the model adjusted for SO_2 and O_3 respectively, a 10 µg/m^3 of $PM_{2.5}$ on lag1 had a RR of 1.011 (1.002–1.021) for all psychiatric diseases and a RR of 1.015 (95%CI 1.003–1.029) for neurotic, stress-related including somatoform disorders (Kim *et al.,* 2019). This was a moderate quality study because despite, data was collected from 51 hospitals and various pollutants were investigated, only meterological variables (temperature, humidity, air pressure, day of the week) were considered.

2.3.11.2 Hospital Visits and Other Contact with Mental Health Professionals

In total eight studies had an outcome of different types of hospital visits and other contact with mental health professionals:

- **Outpatient visits** in three studies (Lu *et al.,* 2020; Li *et al.,* 2020; Lowe *et al.,* 2021),
- **Hospital admissions** in three studies (Chen *et al.,* 2018b; Qui *et al.,* 2019; Wu *et al.,* 2020)
- **Various types** of contact with mental health services *e.g.,* inpatient, outpatient, medical procedures, prescription medication records and emergency department records (Khan *et al.,* 2019) and **inpatient, home treatment team** and **CMHS** in another study (Newbury *et al.,* 2021)

2.3.11.2.1 Outpatient Visits

Three studies conducted in various Chinese cities investigated exposure to air pollutants and outpatient visits for mental health disorders in two time-series studies (Li *et al.,* 2020; Lowe *et al.,* 2021) and one case-crossover study (Lu *et al.,* 2020).

Outpatient records were from two hospitals in Nanjing to investigate daily $PM_{2.5}$ and PM_{10} exposure (Lowe *et al.,* 2021). Significant positive associations were demonstrated on the same day (lag0) and the average over the same day including the previous day (lag0:1). Each 10 µg/m^3 increase on lag0 of $PM_{2.5}$ was associated with a 0.40% increase (95% CI: 0.07-0.72) in psychiatric visits and for PM_{10} a 0.31% increase (95% CI: 0.09-0.54). However, negative significant associations were found for average

PM_{10} three days prior (lag3) and psychiatric visits. In the exposure response curves there was a linear relationship between increasing PM concentrations from 0 to 150 μg/m^3 (Lowe *et al.,* 2021). Although, the uncertainty around the estimates increased particularly at high concentrations, likely due to sparse data (Lowe *et al.,* 2021). Concentration-response threshold was not observed below which no excess psychiatric visits would be expected. When SO_2, NO_2 and CO were added to the PM_{10} and $PM_{2.5}$ model the association remained positive but was reduced to non-significance (Lowe *et al.,* 2021). The association was affected by age and sex. Those aged over 65 were found to be at higher relative risk compared to younger individuals (5-64). For example, 10 μg/m^3 increases in $PM_{2.5}$ were associated with 1.75% (95% CI: 1.26-2.25) increases in visits for the 65+ age group, compared to 0.10% (95% CI: -0.18-0.39) increases for the 5- to 64-year age group (Lowe *et al.,* 2021). Higher relative risks were also observed for male versus female patients, 10 μg/m^3 increases in $PM_{2.5}$ and PM_{10} were associated with 0.80% (95% CI: 0.45-1.14) and 0.61% (95% CI: 0.37-0.85) increase for male patients, compared to 0.12% (95% CI: -0.19-0.43) and 0.10% (95% CI: -0.11-0.31) for females (Lowe *et al.,* 2021). The differences for cold, versus warm weather were not statistically significant but the relative risks were higher for cold weather (Lowe *et al.,* 2021). A similar time-series study conducted in three Chinese cities showed the number of daily outpatient visits for mental disorders increased with higher air pollutant concentrations (PM_{10}, $PM_{2.5}$, SO_2, NO_2) (Li *et al.,* 2020). $PM_{2.5}$ only exhibited significant effects at lag0 in Shenzhen (Excess Risk [ER] = 1.20%, 95% CI: 0.28%-2.13%) (Li *et al.,* 2020). The effects of PM_{10} on mental disorders was significant at lag0 in Shenzhen (ER = 0.99%, 95% CI: 0.36%-1.62%) and Zhaoqing (ER = 0.68%, 95% CI: 0.04%-1.33%) (Li *et al.,* 2020). Significant positive associations for 10 μg/m^3 increases in NO_2 at lag03 were found in all three cities for mental disorders; 4.45% (95% CI: 2.90%, 6.04%) in Huizhou, 7.94% (95% CI: 6.28%, 9.62%) in Shenzhen, and 2.19% (95% CI: 0.51%, 3.89%) in Zhaoqing (Li *et al.,* 2020). For SO_2, lag patterns varied across cities. The ER was 2.62% (95% CI: 0.55%, 4.74%) in Huizhou at lag3 and 10.74% (95% CI: 3.20%, 18.84%) in Shenzhen at lag0 which was significant (Li *et al.,* 2020). Additionally, association varied by the mental health condition. For anxiety, effects of $PM_{2.5}$, PM_{10} and SO_2 were found to only be significant in Shenzhen, while the effects of NO_2 were significant in all three cities (Li *et al.,* 2020). Affective disorders were non-significantly associated with SO_2, while the other pollutants showed significant results. Only $PM_{2.5}$ was non-significantly associated to schizophrenia. There were also variations in terms of sex and age. Generally, males compared to females were more sensitive to ambient air pollution although this was only significant in Zhaoqing for PM_{10} (Li *et al.,* 2020). Moreover, associations were more pronounced in adults than in people younger than 18 years old (Li *et al.,* 2020).

Both studies controlled for meterological (*e.g.,* temperature and humidity) and time variables (calendar time). However, not important factors such as socioeconomic status and deprivation. The study by Li and colleagues was described as moderate whereas the study by Lowe and colleagues was described as low-moderate. This is because Li and colleagues investigated various pollutants as well as overall mental disorders and the type of disorder in various cities. In contrast Lowe and colleagues only investigated overall psychiatric disorders in one city.

A time-stratified case-crossover study conducted in China, collected data from 13 of the largest hospitals and demonstrated positive associations for 10 μg/m^3 increases in all pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3) at different lags (lag0-5) (Lu *et al.,* 2020). The cumulative effects of all pollutants tended to be stable at lag05 therefore, stratified analyses were performed at lag05 day for all pollutants. The percentage of hospital outpatient visits attributable to the air pollutants at lag05 was 4.49% (95% CI: 2.1–6.8%) for $PM_{2.5}$, 3.91% (95% CI: 1.14–6.59%) for PM_{10}, 14.99% (95% CI: 11.34–18.47%) for NO_2, 3.34% (95% CI: 1.12–5.48%) for SO_2, and 4.38% (95% CI: 0.7–7.9%) for O_3 (Lu *et al.,* 2020). The effects of air pollutants on hospital outpatient visits varied for cause-specific mental disorders. Anxiety was significantly associated with $PM_{2.5}$, NO_2, and SO_2 (Lu *et al.,* 2020). Although, NO_2 was the only pollutant associated with other subtypes of mental disorders (schizophrenia, bipolar disorder, obsessive-compulsive) (Lu *et al.,* 2020). In the two-pollutant model at lag05 days, the effects of NO_2 were robust when controlling for $PM_{2.5}$ or PM_{10}. However, the effect of $PM_{2.5}$ and PM_{10} became insignificant after controlling NO_2. The associations varied by pollutants in terms of sex, age, and season. $PM_{2.5}$, PM_{10}, NO_2 and SO_2 demonstrated significant effects on outpatient visits in males. The effects of $PM_{2.5}$, NO_2 and O_3 were significant in females. In the 35–64-year-old age group, hospital outpatient visits for mental disorders were positively associated with $PM_{2.5}$, PM_{10}, NO_2, and SO_2. In 65+ age group positive associations were found for $PM_{2.5}$, NO_2 and O_3. In cold season, $PM_{2.5}$, PM_{10}, NO_2 and SO_2 were significantly associated with outpatient visits. Whereas the effect of O_3 was significant in warm season (Lu *et al.,* 2020).

This study was described as moderate/high quality because the study design controls for time (same day of the week, month, and year), meterological variables (temperature, humidity, wind speed) as well as short-term time invariant potential confounders, such as age, sex, smoking status, and deprivation (Peters *et al.,* 2006). Moreover, various pollutants were investigated, and the study was large (111,842) although there were no descriptive statistics. In addition, the fixed sites of air monitoring stations used in all three studies may not reflect patient's actual exposure.

2.3.11.2.2 Hospital Admissions

Three time-series studies in three different Chinese cities investigated air pollution exposure and mental health hospital admissions (Chen *et al.,* 2018b; Qui *et al.,* 2019; Wu *et al.,* 2020).

Daily hospital admission from a large city in China and daily exposure to various pollutants (NO_2, SO_2, CO, O_3, PM_{10}, $PM_{2.5}$) were investigated (Chen *et al.,* 2018b). Statistically significant positive association were found for 10 μg/m^3 increases in pollutants and daily hospital admissions for PM_{10} 1.27% (95% CI: 0.28%, 2.26%), SO_2 6.88% (95% CI: 2.75%, 11.00%) and CO 0.16% (95% CI: 0.02%, 0.30%) on the current- and previous-day (lag 01 day) (Chen *et al.,* 2018b). Positive but insignificant associations were found for 10 μg/m^3 increases in pollutants and hospital admissions for $PM_{2.5}$ 1.09% (95% CI: –0.10%, 2.28%), NO_2 1.88% (95% CI: –0.40%, 4.16%) and O_3 0.34% (95% CI: –1.08%, 1.75%) (Chen *et al.,* 2018b). The estimated association of SO_2 remained significant after adjustment for simultaneous exposure to the other pollutants (Chen *et al.,* 2018b). Whereas the associations of PM_{10} and CO were statistically significant only when controlling for O_3. Generally stronger associations were found in warm seasons than in cool seasons. Differences in sex and age had no significant effects on the associations.

Another study found that increasing concentrations of PM_{10} and $PM_{2.5}$ increased mental disorders significantly at lag1, lag2 and all cumulative lags, with the largest effects on lag06 (Qui *et al.,* 2019). A 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10} at lag06 were associated with a 2.89% (95% CI: 0.75–5.08%) and 1.91% (95% CI: 0.57–3.28%) increment in daily hospital admissions, respectively (Qui *et al.,* 2019). In the two-pollutant models effect estimates on mental disorders were generally elevated and significant on lag06 after adjustment for SO_2, NO_2, CO and O_3, except for the associations with $PM_{2.5}$ when NO_2 was included (Qui *et al.,* 2019). The mental disorder with the largest estimates was schizophrenia at lag0, lag1 and all the cumulative lag days. Increases in $PM_{2.5}$ and PM_{10} (10 μg/m^3) at lag06 was associated with a 4.91% (95%CI: 0.51–9.50%) and 3.44% (95%CI: 0.68–6.28%) increase in schizophrenia hospital admissions, respectively (Qui *et al.,* 2019). Stronger associations were demonstrated in males and in cool seasons than in females and in warm seasons (Qui *et al.,* 2019). Using WHO's air quality guidelines as the reference concentrations, 9.53% (95% CI: 2.67–15.58%) and 9.17% (95% CI: 2.91–14.70%) of hospital admissions for mental disorders could be attributable to $PM_{2.5}$ and PM_{10}, respectively (Qui *et al.,* 2019). A substantial burden was caused by PM on schizophrenia. Approximately 15.13% (95% CI:1.83–25.4%) and 15.32% (95% CI:3.49–24.56%) of schizophrenia admissions were estimated to be attributed to $PM_{2.5}$ and PM_{10} respectively, according to the WHO guidelines (Qui *et al.,* 2019).

In Beijing, $PM_{2.5}$ exposure and hospital admissions were significant on lag10, lag11, lag16, with the largest effects on lag11 (Wu *et al.,* 2020). At lag11 a 10 µg/m^3 increase in $PM_{2.5}$ was associated with a relative risk increase (RRI) of 3.55% (95%CI: 0.67%–6.51%) of total mental disorder admissions (Wu *et al.,* 2020). This association remained significant after adjusting for SO_2 and O_3 in the co-pollutant model. However, after adjusting for NO_2 and CO, the RRI was slightly lower than the single pollutant model and showed no significance (Wu *et al.,* 2020). Adjustment for humidity, temperature, wind speed and sunshine duration had no effect. The effects of $PM_{2.5}$ was more pronounced in males (RRI: 3.93% [95% CI: 0.86%– 7.09%], $p<0.05$), elderly (≥65 years old) individuals (RRI: 6.92% [95% CI: 2.74%–11.27%], $p<0.05$) and in cold seasons (RRI: 3.61% [95% CI: 0.46%–6.86%], $p<0.05$) (Wu *et al.,* 2020). Taking WHO's air quality guideline as the reference concentrations, from 2013 to 2015, 15.12% of hospital admissions (2,609 person-times out of 17,252 person-times) could be attributable to exceeding $PM_{2.5}$ concentrations (Wu *et al.,* 2020).

All these time-series studies were described as moderate quality, since, despite controlling for meterological (*e.g.,* temperature and humidity) and time variables (time trend and day of the week) important factors such as socioeconomic status and deprivation were not controlled for. A positive factor was all studies had many participants (>10,000).

2.3.11.2.3 Various Mental Health Service Contact

Two cohort studies explored exposure to multiple pollutants and various mental health contact in London boroughs (Newbury *et al.,* 2021) and the US as well as Denmark (Khan *et al.,* 2019).

Newbury and colleagues used electronic records of individuals aged ≥15 years who had first contact with the South London and Maudsley National Health Service (NHS) Foundation Trust (SLaM) for psychotic and mood disorders in 2008–2012 (n= 13,887). In-patient days and community mental health service (CMHS) events were recorded over 1-year and 7-year follow-up periods. Quarterly increases in NO_2, NO_x, $PM_{2.5}$ and PM_{10} were associated with more in-patient days and CMHS events across follow-up (Newbury *et al.,* 2021). After full covariate adjustment (seasonal fluctuations, annual trends, sex, ethnicity, age, marital status, population density, deprivation, ethnic density, social fragmentation at initial presentation), IQR increases in NO_2, NO_x and $PM_{2.5}$ were significantly associated with 18% (95% CI 4–34%), 18% (95% CI 4–34%) and 11% (95% CI 3–19%) increased risk of inpatient days respectively at 1-year follow-up (Newbury *et al.,* 2021). Furthermore, IQR increases in NO_2, NO_x, $PM_{2.5}$ and PM_{10} were significantly associated with 32% (95% CI 25–38%), 31% (95% CI 24–37%), 7% (95% CI 4–11%) and 9% (95% CI 5–14%) increased risk of CMHS events respectively at 1- year follow-up (Newbury *et al.,* 2021). The results were of comparable magnitude, but associations were more robust for CMHS events than for in-patient days in terms of the precision of confidence intervals and resistance to covariate adjustment (Newbury *et al.,* 2021). Associations were strongest in magnitude for NO_2 and NO_x and persisted at 7-year follow-up (Newbury *et al.,* 2021). Higher concentrations of NO_2 increased risk for CMHS events after 1 year. Individuals in the second (<39.41 μg/m^3), third (<48.08 μg/m^3) and fourth quartiles (≥48.08 μg/m^3) (versus the first quartile <32.65 μg/m^3) of NO_2 had a 16% (95% CI 10–23%), 32% (95% CI 22–42%) and 48% (95% CI 36–62%) increased risk. An analysis by Newbury and colleagues suggested that if the population-weighted $PM_{2.5}$ (13.4 μg/m^3 in 2019) in the four South London boroughs was reduced by 3.4 μg/m^3 to the WHO's recommended annual limit (10 μg/m^3), then annual in-patient and CMHS use could be reduced by 2.9% (95% CI 0.9–5.8%) and 2.0% (95% CI 1.0–2.9%) respectively.

This was a high-quality study because important confounders were controlled for such as seasonal fluctuations, annual trends in air pollution concentrations and psychiatric admissions, ethnicity, deprivation, and social fragmentation. In addition to a reliable diagnosis of mental health (ICD-10), large population (13887) and participants were followed up from 1 year to 7 years.

Khan and colleagues investigated the effects of air quality in the US on schizophrenia, bipolar disorder, and personality disorders. In addition to multiple pollutants (NH_4, NO_3, NO_X, SO_4, elemental and organic carbon, secondary inorganic aerosols, as well as CO, NO_2, O_3, PM_{10}, $PM_{2.5}$, SO_2) in Denmark on these conditions. The associations were investigated in the US cohort, in Denmark cohort and combined. The strongest predictor for bipolar disorder diagnosis, after a population's ethnicity composition, was air quality in the US. The worst air quality was associated with an approximately 27% increase (95% credible interval [CrI] 15%–40%, p_{MCMC}<10−4) in the apparent rate of bipolar disorder (Khan *et al.,* 2019). Air quality was not a strong predictor for schizophrenia or personality disorder in the US. Whereas, in Denmark, the rate of all psychiatric disorders increased with increasing levels of exposure to air pollution. The estimated rate of schizophrenia was 148% higher (95% CI 119%–180%, p < 2 × 10−16) among individuals in the group with the highest exposure to air pollution (Q7) compared with those with the least exposure (Q1, the referent group) (Khan *et al.,* 2019). Estimated rate of bipolar disorder was 29.4% higher (95% CI 9.4%–52.9%, p < 3 × 10−3) and 24.3% higher (95% CI 4.5%–47.9%, p < 0.014) in the exposure categories Q6 and Q7, respectively, compared with Q1 (Khan *et al.,* 2019). The strongest association was between air pollution and personality disorder, showing a 162% increase (95% CI 142%–183%, p < 2 × 10−16) in the disorder rate among category Q7 compared with category Q1. When considering the adjustment variables, the trend of association remained comparable (Khan *et al.,* 2019). The authors demonstrated correlation signals between air pollution and bipolar disease in both countries and between air pollution and schizophrenia, as well as personality disorder in Denmark. In the harmonised data the rate increases in the highest exposure group (Q7) compared to the least-exposure group (Q1) were as follows: bipolar disorder 31.4% (95% CI 7.4%–60.8%, $p= 0.007$), schizophrenia 104.3% (95% CI 76.3%–136.8%, $p < 2 \times 10{-}16$), and personality disorder 209.6% (95% CI 183.5%–238%, $p < 2 \times 10{-}16$) (Khan *et al.,* 2019).

The quality of this study was described as moderate to high because both datasets were large scale, in addition income, and sex were controlled for. The US data set also controlled for percentages of poor and insured population as well as ethnicity. Although, the Denmark dataset controlled for various socioeconomic confounders, such as urbanicity, parental educational level, parental employment as well. Both datasets had limitations, strengths, and biases. The use of data from multiple countries could be more representative however countries will have different cultures, with diverging approaches to healthcare (diagnoses), population tracking, and environmental monitoring. Therefore, harmonising the data could be affected by various confounding variables.

The information in this section is summarised in tables below (**Tables 2.25-2.30**).

2.3.11.3 Summary of Contact with Mental Health Professionals and Pollution Associations

The associations will be summarised below in four different tables titled:

- Emergency department visits
- Outpatient visits
- Hospital admissions
- Various mental health service contact

Emergency Department Visits

The associations between emergency department visits for multiple diagnosed conditions and various pollutants investigated in the paragraph named emergency department visits are summarised in **Table 2.25** below.

Table 2.25- Summary of the associations found between various pollutants and emergency department visits.

Pollutant exposure & source	Association of the Pollutant with Emergency Department Visits	Reference	Key Findings	Conclusions
$PM_{2.5}$	**Significant positive** to:			Overall, more of the studies found $PM_{2.5}$ was associated to increased emergency department visits. Although, the associations varied by type of disorder and appear to be affected by age. Since negative and positive associations were found it is important that more research is carried out which also considers demographic variables.
	Mental health	(Muhsin *et al.,* 2021)	No association to specific disorders. Increased risk aged 35-65.	
		(Szyszkowicz *et al.,* 2020)	Aged 8-24	
	Mental health & neurotic disorders.	(Nguyen *et al.,* 2021)	Higher risk in 65+ group & self-harm in warm season.	
	All disorders, schizophrenia, suicidality, adjustment & mood disorders.	(Brokamp *et al.,* 2019)	In children, effects of deprivation varied by disorder type.	
	Ambulance dispatches	(Liu *et al.,* 2019)	Higher risk of suicide-related	

			emergencies for children compared to adults & no sex effects.	
	Negative association	(Bernardini *et al.,* 2019)	Regression coefficient -0.009	
	No association to:			
	Mental health disorders	(Kim *et al.,* 2019)	Association found with adjustment for SO_2 & O_3.	
	Anxiety & suicide	(Diaz *et al.,* 2020)	Noise increased risk.	
	Schizophrenia, psychosis & substance use.	(Nguyen *et al.,* 2021)	Non-significant & association type varied by lags.	
PM_{10}	**Significant positive**	(Oudin *et al.,* 2018)	Percentage change 2.3%. Increased in the warm season.	The variation in the associations found for increases in PM_{10} and emergency department visits shows the need for more research to confirm if PM_{10} influences metal health emergencies.
		(Muhsin *et al.,* 2021)	No association to specific disorders. Increased risk for ages 35-65.	
	Negative association	(Bernardini *et al.,* 2019)	Regression coefficient -0.005	
	No association to anxiety & suicide	(Diaz *et al.,* 2020)	Noise increased risk.	
NO_2	**Significant positive** to:			More studies found NO_2 did not increase the risk of emergency visits for mental health disorders. However, clarification is necessary via more research.
	All disorders	(Szyszkowicz *et al.,* 2020)	Males aged 13-118.	
	Neurotic, stress-related & somatoform	(Kim *et al.,* 2019)	RR 1.015	
	Negative association	(Bernardini *et al.,* 2019)	Regression coefficient -0.0010	
	No association to:			

	All disorders	(Oudin *et al.,* 2018)	0.3% (95% CI −0.8–1.5)	
	Anxiety & suicide	(Diaz *et al.,* 2020)	Noise increased risk.	
	All disorders, bipolar, schizophrenia, nor suicide/self-harm	(Thilakaratne *et al.,* 2020)	Reduced risk of suicide/self-harm in the cool season.	
O_3	**Significant positive:**			Associations varied depending on the type of disorder and even between all disorders. Risk also varied in terms of sex in some studies. Due to contrasting findings for research into the effects of O_3 on emergency department visits more research is important.
	Mental health, self-harm/suicide, mood disorders & neurotic disorders.	(Nguyen *et al.,* 2021)	Increased risk for ages 0-18, in warm season & substance use in females.	
	Mental disorders	(Bernardini *et al.,* 2019)	Adjustment for other pollutants had no effect.	
		(Szyszkowicz *et al.,* 2020)	Males aged 13-18.	
		(Kim *et al.,* 2019)	RR 1.039	
	No association:			
	All disorders	(Oudin *et al.,* 2018)	0.1% (95% CI −0.6–0.9)	
	Anxiety & suicide	(Diaz *et al.,* 2020)	Noise increased risk.	
	Schizophrenia, psychosis, & substance use	(Nguyen *et al.,* 2021)	Non-significant & association type varied by lags.	
SO_2	**Significant negative** to all disorders	(Kim *et al.,* 2019)	RR 0.991	Only one study so more evidence is needed to come to conclusions.
CO	**Significant negative**	(Bernardini *et al.,* 2019)	Regression coefficient -0.690, p<0.1	CO may not increase the risk of emergency department visits.

		(Kim *et al.,* 2019)	RR 0.966	Although, only three studies found this so more research is required to confirm if CO is not a risk factor for mental health disorder emergencies.
	No association to mental disorders, bipolar, schizophrenia, nor suicide/self-harm.	(Thilakaratne *et al.,* 2020)	Reduced risk of mental disorders & suicide/self-harm in cool season.	

- Positive associations and no association were demonstrated for most pollutants.
- The largest number of studies investigated $PM_{2.5}$ which could have a negative impact on mental health emergencies.

The quality assigned to the studies in this section is summarised in **Table 2.26** below.

Table 2.26- Study quality described in the table below.

Quality	**Study Citation**
Moderate	(Bernardini *et al.,* 2019; Kim *et al.,* 2019; Liu *et al.,* 2019; Diaz *et al.,* 2020; Thilakaratne *et al.,* 2020; Nguyen *et al.,* 2021)
Moderate/high	(Oudin *et al.,* 2018; Brokamp *et al.,* 2019; Szyszkowicz *et al.,* 2020; Muhsin *et al.,* 2021)

Outpatient Patients

The associations between outpatient visits for multiple diagnosed conditions and various pollutants investigated in the paragraph named outpatient visits are summarised in **Table 2.27** below.

Table 2.27- Summary of the associations found between various pollutants and outpatient visits in Chinese cities.

Pollutant exposure and source	Association of Pollutant with Outpatient Visits	Reference	Key Findings	Conclusions
Short-term $PM_{2.5}$	**Significant positive** associations	(Lowe *et al.*, 2021)	Higher risk for males and those aged >65 compared to 5-64. Association remined positive but became insignificant when SO_2, NO_2 & CO were included.	$PM_{2.5}$ was found to have negative effects on out-patient visits. However, these associations varied depending on the mental health condition & those at higher risk varied depending on the pollutant.
		(Li *et al.*, 2020)	ER 1.20%. Higher risk for adults (≥18 years) & males.	
		(Lu *et al.*, 2020)	ERR 4.49%. Became insignificant when NO_2 was included. Associations varied by pollutants in terms of sex, age, and season.	
	No association to schizophrenia	(Li *et al.*, 2020)	Associations found for PM_{10}, SO_2, NO_2	
Short-term PM_{10}	**Significant positive** associations	(Li *et al.*, 2020)	Lowest ER of all pollutants (0.99% & 0.68%).	PM_{10} could be a risk factor for outpatient visits

		(Lowe *et al.,* 2021)	A 0.4% increase compared to 0.31% for $PM_{2.5.}$ Inclusion of SO_2, NO_2 & CO caused the association to become non-significant but remained positive.	although other pollutants had stronger associations.
		(Lu *et al.,* 2020)	ERR 3.91%. Became insignificant when NO_2 was included.	
NO_2	**Significant positive** associations	(Li *et al.,* 2020)	Only pollutant with significant associations in all three cities.	NO_2 may be an important risk factor for outpatient visits since associations were more consistent, did not vary between mental disorders & was not affected by co-exposure.
		(Lu *et al.,* 2020)	Highest ERR (14.99%). Associated to all subtypes. Not affected by co-exposure ($PM_{2.5}$ or PM_{10}).	
SO_2	**Significant positive** associations	(Li *et al.,* 2020)	Highest ER in Shenzhen (10.74%).	SO_2 was found to have a negative effect on mental health in two studies. Although this varied between conditions.
		(Lu *et al.,* 2020)	ERR 3.34%	
	No association to affective disorders	(Li *et al.,* 2020)	Associations found for other pollutants (PM_{10}, $PM_{2.5}$, NO_2).	
O_3	**Significant positive**	(Lu *et al.,* 2020)	ERR 4.38%	Only one study so more evidence is needed to clarify the effects of O_3.

- NO_2 had the most notable effect on outpatient visits.

The quality assigned to the studies in this section is summarised in **Table 2.28** below.

Table 2.28- Study quality described in the table below.

Quality	**Study Citation**
Low/moderate	(Lowe *et al.,* 2021)
Moderate	(Li *et al.,* 2020; Lu *et al.,* 2020)

Hospital Admissions

The associations between hospital admissions for multiple diagnosed conditions and various pollutants investigated in the paragraph named hospital admissions are summarised in **Table 2.29** below.

Table 2.29- Summary of the associations found between various pollutants and hospital admissions in Chinese cities.

Pollutant exposure & source	Association of Pollutant with Admissions	Reference	Key Findings	Conclusions
Daily $PM_{2.5}$	**Significant positive**	(Qui *et al.,* 2019)	2.89% for 10 μg/m^3 increase. Associations became insignificant when NO_2 was included. Largest risk for schizophrenia (4.91%). Strongest association in males & cool season.	$PM_{2.5}$ concentration increases could be a risk factor for hospital admissions particularly schizophrenia. Being male & the season could put individuals more at risk. However more research is needed to clarify this due to contrasting findings.
		(Wu *et al.,* 2020)	Attributable to 15.2% of admissions. Higher risk in males, aged >65 & cool season. Association remained significant after adjustment for SO_2 & O_3, not NO_2 & CO.	
	Positive association	(Chen *et al.,* 2018b)	1.09% for 10 μg/m^3 increase. Significant differences not found for age & sex. Risk increased in the warm season.	
Daily PM_{10}	**Significant positive**	(Chen *et al.,* 2018b)	1.27% for 10 μg/m^3 increase. Significant	Positive associations were also found for daily PM_{10} &

			when controlling for O_3 only.	hospital admissions. But the lack of literature means further clarity is necessary.
		(Qui *et al.,* 2019)	1.91% for 10 μg/m^3 increase. Largest risk for schizophrenia (3.44%).	
Daily NO_2	**Positive association**	(Chen *et al.,* 2018b)	1.88% for 10 μg/m^3 increase.	NO_2 had a negative effect on mental health but further clarity is needed through research.
Daily SO_2	**Significant positive**	(Chen *et al.,* 2018b)	Highest increase (6.88% for 10 μg/m^3 increase). Not effected by co-exposure.	SO_2 had the most negative effect on mental health but further clarity is needed through research.
Daily CO	**Significant positive**	(Chen *et al.,* 2018b)	0.16% for 10 μg/m^3 increase. Significant only when controlling for O_3.	CO had a negative effect on mental health, but further clarity is needed through research.
Daily O_3	**Positive**	(Chen *et al.,* 2018b)	0.34% for 10 μg/m^3 increase.	O_3 had a slight negative effect on mental health but further clarity is needed through research.

- Daily exposure increased hospital admissions however the lack of research means more evidence is necessary.
- All three studies investigated $PM_{2.5}$ exposure.

The quality assigned to the studies in this section is summarised in **Table 2.30** below.

Table 2.30- Study quality described in the table below.

Quality	**Study Citation**
Moderate	(Chen *et al.,* 2018b; Qui *et al.,* 2019; Wu *et al.,* 2020)

Various Mental Health Service Contact

The associations between various mental health service contact for multiple diagnosed conditions and various pollutants investigated in the paragraph named various mental health service contact are summarised in **Table 2.31**.

Table 2.31- Summary of the associations found and not found between various pollutants and various mental health service contact.

Pollutant exposure and source	Association of the Pollutant with Increased Risk of …	Reference	Key Findings	Conclusions
NO_2 & NO_x	In-patient days and CMHS events	(Newbury *et al.,* 2021)	Dose response relationship. Not affected by sex, age, ethnicity, and deprivation. Highest risk (18%) & persisted at 7-year follow-up	Only one study had this outcome, so more research is needed. Although as shown in outpatient visits NO_2 could be an important risk factor.
$PM_{2.5}$	In-patient days and CMHS events	(Newbury *et al.,* 2021)	Reduced risk (11%).	Negative effect found but reduced risk compared to NO_2.
Worse air quality	Bipolar in US. Bipolar, schizophrenia, and personality disorder in Denmark. Not for schizophrenia or personality disorder in the US.	(Khan *et al.,* 2019).	Ethnicity was the strongest predictor of bipolar disorder in the US then air quality. Association varied by type of disorder	Worse air quality appeared to have a negative effect on mental disorders however this was affected by the country & disorder. So, more research is required to clarify these associations.

- Worse air quality, $PM_{2.5}$, NO_2 and NO_x had a negative impact on various mental health outcomes, and these varied depending on the condition.

The quality assigned to the studies in this section is summarised in **Table 2.32** below.

Table 2.32- The quality of the studies is described below.

Quality	**Study Citation**
Moderate/high	(Khan *et al.,* 2019)
High	(Newbury *et al.,* 2021)

2.4 Discussion

The objective of this study was to determine if there was an association between different air pollutants/air quality and mental health together with well-being. Whilst considering demographic variables such as deprivation. In the 87 articles selected the impact of short- and long-term air pollution on various mental health conditions and well-being issues was investigated:

- Psychotic disorders
- Suicide related
- Mania
- Self-harm
- Anxiety
- Mortality linked to mental health
- Self-reported mental health and well-being
- Psychological stress and distress
- Contact with mental health services

The effects of air pollution on depression were not explored in this review since a recent comprehensive systematic review and meta-analysis had already explored this (Borroni *et al.,* 2021).

In this review associations varied for different pollutants and mental health outcomes, including between studies and within a study. Many studies demonstrated air pollution had a negative impact on various mental health outcomes. However, some studies also found no association. Moreover, three studies found increases in different pollutants (NO_2, O_3, $PM_{2.5}$, PM_{10}, CO) improved mental health (Bakolis *et al.,* 2020; Bernardini *et al.,* 2019; Zock *et al.,* 2018). For the mental health outcomes, anxiety, suicide, and contact with mental health services, positive as well as no association was found in almost equal quantities of the studies. The outcomes, mania, self-harm, and mortality linked to mental health lacked research evidence, so it was not possible to come to reliable conclusions. In terms of the self-reported mental health outcomes more research is necessary as the findings in this review were inconclusive and contradictory.

The two key findings observed were the positive associations between PM and NO_2 on stress and psychotic disorders. This was shown by the number of studies and the lack of contrasting findings. The most hazardous pollutants to self-reported stress were $PM_{2.5}$ and NO_2. The highest OR (2.91) was in men aged 30-64 in the co-pollutant model (NO_2 and PM_{10}) when concentrations were higher than 30.08 ppb in the most stressed category (Hwang *et al.,* 2018). Furthermore, four studies used the same questionaire (Kessler Psychological Distress Scale) and demonstrated a significant positive association between $PM_{2.5}$ and distress (Gu *et al.,* 2019; Klompmaker *et al.,* 2019; Pinault *et al.,* 2020).

Stress is recognized as an important risk factor for impaired mental health, however not all people who experience stress, experience impaired mental health (Newnham *et al.,* 2015; Schönfeld *et al.,* 2016). Moreover, the cumulative effects of daily stressors are important predictors for the emergence of symptoms of depression and anxiety (D'Angelo & Wierzbicki, 2003; Parrish *et al.,* 2011). However, assumptions that merely include direct effects of stress on health are incomplete and ignore possible intervening or mitigating factors, leading to a potentially inaccurate estimation of effect sizes (Schönfeld *et al.,* 2016). The strength of the association between stress and mental state depends on characteristics and strategies that differentiate individuals from one another (Leiva-Bianchi *et al.,* 2012). Furthermore, experimental evidence has shown that air pollution, can activate the HPA axis and release cortisol (stress hormone) (Li *et al*; 2017; Hajat *et al.,* 2019; Thomson, 2019; Thomson *et al.,* 2021). This further supports a potential link between increased air pollution and stress. Although more research is needed to explore if air pollution could increase stress and therefore potentially the risk of mental disorders. However, for the outcome stress/distress there was less research, and the outcome was self-rated not clinically diagnosed. Therefore, psychotic disorders were the most noted mental health effect in this review.

As previously discussed $PM_{2.5}$, PM_{10} and NO_2 appeared to negatively affect psychotic disorders. These associations were found in seven studies for $PM_{2.5}$ and nine for PM_{10}. For both pollutants two studies did not find an association- $PM_{2.5}$ (Antonsen *et al.,* 2020; Li *et al.,* 2020) and PM_{10} (Antonsen *et al.,* 2020; Nguyen *et al.,* 2021). The highest number of studies (ten) found an association between psychotic disorders and NO_2 (Tong *et al.,* 2016; Duan *et al.,* 2018; Bai *et al.,* 2019; Horsdal *et al.,* 2019; Liang *et al.,* 2019; Newbury *et al.,* 2019; Antonsen *et al.,* 2020; Li *et al.,* 2020; Lu *et al.,* 2020; Lee *et al.,* 2022). However, one study found there was no association between schizophrenia and NO_2 (Thilakaratne *et al.,* 2020). Therefore, overall, NO_2 appeared to be the biggest risk factor for psychotic disorders. The pollutant, NO_2, is closely correlated with heavy traffic and diesel vehicle emissions (Newbury *et al.,* 2021). The highest association between NO_2 at a concentration of 26.0 $\mu g/m^3$ and psychosis was OR 1.71 in adolescents (Newbury *et al.,* 2019). In addition to a RR of 1.84 (Duan *et al.,* 2018) and 1.88% increase in schizophrenia hospitalisation (Liang *et al.,* 2019). Although, these associations varied by age group (adolescents or >65 years old), outcome (severity, relapse, hospitalisation for psychosis or schizophrenia), study design (time-series or cohort or case-crossover), time periods (long- and short-term) and geographical location (Chinese cities or Denmark or UK).

Moreover, the association appeared not to be affected by demographic variables such as socioeconomic factors (Bai *et al.,* 2019; Newbury *et al.,* 2019). This was not supported by the hypothesis. Furthermore, due to the potent oxidising and inflammatory properties of air pollutants it has been proposed that these pollutants could affect the brain directly by translocating along the olfactory nerve and permeating the blood–brain barrier and/or indirectly by eliciting systemic inflammation (Block & Calderón-Garcidueña, 2009). Neuroinflammation and oxidative stress are likewise both implicated in the aetiology of psychotic disorders (Fraguas *et al.,* 2019). Therefore, a role of air pollution exposure in the severity and course of psychotic disorders is biologically plausible. Therefore, this evidence further supports the findings that NO_2 could have a negative impact on psychotic disorders.

Although, these findings are still inconclusive particularly since the studies were heterogenous in terms of exposure periods, study design, participants, geographical locations, and settings as discussed above, including the lack of a confirmed causal mechanism. This further complicates elucidating if air pollution has negative impact on psychotic disorders or other mental health conditions. Therefore, psychotic disorders were the chosen mental health outcome for the SAIL analysis (data chapter 2) to investigate if these findings would support the negative impact of $PM_{2.5}$, PM_{10} and NO_2 found in the review.

2.4.1 Limitations, Knowledge Gaps and Future Recommendations

A key strength of this review is the comprehensive and systematic approach taken according to PRISMA guidelines. In addition, title and abstract screening was completed by two authors and the third author resolved any disagreements. Quality assessment was also implemented by AM who completed data extraction and quality assessment on five articles which were compared to EC's work. Standardized data extraction and quality assessment procedures were also used. Furthermore, a much broader range of mental health outcomes (self-reported and diagnosed as well as diverse types) were assessed compared to previous reviews in this area. In addition to the investigation of different exposure periods and pollutants. However, this review also had limitations.

Some of the limitations of this systematic review which are also relevant to the research area are written in **Table 2.33** below. One of the biggest limitations was the heterogeneity of the studies. Future recommendations are also identified in **Table 2.33** below in terms of more robust methodology and knowledge gaps.

Table 2.33- Identifies limitations and explains any future recommendations.

Limitations	Explanation of Limitations	Future Recommendations
Between-study heterogeneity was high, resulting in: - No meta-analysis - Difficulty summarising & comparing results.	A meta-analysis uses statistical methods to summarise results of studies in a systematic review (Ioannidis *et al.,* 2008). This was not performed in this review because of the high heterogeneity between studies. For example, differences in exposure periods, pollutants, mental health outcomes, study designs, participants, geographical locations, and settings. High heterogeneity between studies or poor methodology can cause meta-analyses to be misleading (Deeks *et al.,* 2022; Ioannidis *et al.,* 2008).	Standardised and recommended research methods such as the best exposure period to investigate (Hahad *et al.,* 2020).
Lack of specific quality assessment tool for air pollution exposure and mental health studies	The JBI tool is not specifically tailored to environmental epidemiology studies investigating air pollution and mental health. Therefore, not all the questions asked by the tool were relevant to the research area which could result in bias in this study.	More specific quality assessment tools for this area of research.
Subjective quality assessment	Quality assessment using JBI tool required a degree of judgment so could reflect the authors subjective opinion, for example, some of the questions asked: - 'Was the exposure and outcomes measured in a valid and reliable way?' - 'Were confounding factors identified and controlled for?' The question above is particularly challenging because of incomplete knowledge about the influence of confounding variables and which are important to consider. This could result in differences in opinion on the quality of papers.	A less subjective quality assessment tools.

Only correlational evidence and the unknown causal mechanism.	Analysing new evidence requires statistical and clinical knowledge (Hung *et al.,* 2017). Studies in this area have only correlational evidence and therefore lack clinical knowledge (Hung *et al.,* 2017). It is necessary not to overemphasize the statistical significance without consideration of effect size and whether differences could be considered clinically meaningful (Hung *et al.,* 2017).	More research into the potential causal mechanisms of the association (Misiak, 2020, Bakolis *et al.,* 2021; Hahad *et al.,* 2020).
Residual and unmeasured confounding	There are many potential confounders that could affect the association and are difficult to control for: - **Psychological factors** (*e.g.,* life events, compliance to treatment, and poor social support) (Dattani *et al.,* 2021), - **Socioeconomic status** (Bernardini *et al.,* 2019; Generaal *et al.,* 2019), - **Green space** (Kumar *et al.,* 2019; Lauwers *et al.,* 2020) which was only considered in one study (Generaal *et al.,* 2019). Some degree of residual confounding can be found even in well-controlled studies such as Antonsen *et al.* (2020), Bakolis *et al.* (2020) and Pun *et al.* (2017). Since, the relationship between socioeconomic status and mental health, varies across disorder types, and is further complicated by individual-level characteristics including genetics, sex, and ethnicity (CDC, 2004). Moreover, these associations are not fully understood (CDC, 2004).	More research investigating how confounding factors such as deprivation could affect any potential association (CDC, 2004).
Categorising the mental health outcomes to assist in understanding any associations.	Categorisation was challenging due to: - Diverse range of mental health outcomes at clinical and subclinical endpoints. - Multiple self-reported mental health outcomes.	Clear and global definition of mental health and more research into sub-clinical endpoints.

	- Some questionnaires can be used for multiple conditions due to overlapping symptoms such as Hospital Anxiety and Depression Scale (Clark *et al.,* 2017). - Studies describing the mental health outcome differently to what the clinical questionaire is often used for.	
Reliability & accuracy of mental health outcomes.	There are biases in mental health data: - Underreporting of suicide (Katz *et al.,* 2015) - Potentially undercounted in emergency departments, because coders may only record the primary diagnosis (Steele *et al.,* 2004; Braithwaite *et al.,* 2019). - Approximating outcome incidence with hospital attendance (Braithwaite *et al.,* 2019). These biases may limit generalisability, although routine data (hospital admissions) represents some of the most complete data available (Braithwaite *et al.,* 2019).	Supports the recommendation above of better understanding of defining mental health. In addition to encouraging parity of esteem between physical and mental health.
Assessment of air pollution exposure (Hahad *et al.,* 2020)	Despite, 58% of the studies in this systematic review used stationary monitors, this technique can make it difficult to measure individual exposure due to varying proximities and sparse locations of monitors (Hahad *et al.,* 2020; Bhui *et al.*, 2023). Moreover, most studies only considered exposure at participants residence apart from two studies. Newbury *et al*. (2019) measured air pollution at participants' residence and two commonly visited locations. Choi *et al*. (2020) considered classroom, school, and activity-based exposure. Furthermore, different pollutants and concentrations vary	Consideration of variables that affect pollutant concentra-tions and exposure assessment tools with finer spatial and temporal resolution (Briggs *et al.,* 1997; Briggs, 2005; Zhang & Lioy, 2002).

	depending on the location and sometimes time of year (hot summer weather conditions are associated with high ozone concentrations) (UK Government, 2023).	
Lack of adjustment for co-exposure to multiple pollutants	Co-exposure was investigated in 12 studies in this review (Ng *et al.,* 2016; Oudin *et al.,* 2018; Bai *et al.,* 2019; Kim *et al.,* 2019; Qui *et al.,* 2019; Bakolis *et al.,* 2020; Wu *et al.,* 2020; Yue *et al.,* 2020; Zhao *et al.,* 2020; Lowe *et al.,* 2021; Ma *et al.,* 2021; Reuben *et al.,* 2021). This is important as pollutants are often spatiotemporally correlated together (and therefore likely inhaled together) (Braithwaite *et al.,* 2019). Most studies constructed only single-pollutant models, meaning that they could not exclude either confounding or effect modification by other pollutants (Braithwaite *et al.,* 2019).	Consideration of co-exposure to various air pollutants (Braithwaite *et al.,* 2019)
Explanation of non-significant findings is inconsistent.	Some studies describe results without statistical significance as not finding an association whereas others describe finding for example a positive association which was non-significant. This also varied depending on the statistics used. The inappropriate interpretation of statistical results has been shown to be widespread. A study found that 54.2% of trials inappropriately interpreted a result that was not statistically significant as indicating no treatment benefit (Gates & Ealing *et al.,* 2019). Some studies have been shown to place an over-emphasis on statistical significance and not acknowledge uncertainty (Hemming *et al.,* 2022).	When interpreting findings that are non-significant it is imperative that authors consider whether confidence intervals support clinically meaningful effects (Hemming *et al.,* 2022). In addition to power analyses which are balanced with an experimental perspective.

Studies that did not define lags.	The exposure period could be hard to define and understand *e.g.,* if the exposure period was before or after the mental health event.	Clear explanation of how a lag is defined.

Data Chapter 2:

Impact of air pollution on psychotic disorders with consideration of demographic variables: A retrospective data linkage cohort study

Declaration: Jane Lyons (JL) and Amy Mizen (AM) assisted in the SAIL Analysis. JL created the linked cohort which included the Welsh Longitudinal General Practice (WLGP) dataset to identify schizophrenia and other psychotic disorder diagnoses within the study period. AM provided the air pollution data at the LSOA level.

3 Secure Anonymised Information Linkage (SAIL) Pilot study

3.1 Introduction

The Secure Anonymised Information Linkage (SAIL) Databank at Swansea University, contains anonymised longitudinal, routinely collected, health, social, and environmental, data on the Welsh population (Mizen *et al.,* 2020). This population databank contains the Welsh Demographics Service (WDS) dataset, a population register which includes home address histories provided by patients registered with a GP in Wales. The GP service in the UK is free at the point of care. The SAIL Gateway uses a secure virtual environment and remote desktop protocol so that data can be accessed safely anywhere in the world.

Some of the worst air quality in the UK is found in Wales (Howorth, 2021). The main pollutants of concern are $PM_{2.5}$ or PM_{10} and NO_2, which can cause a range of health impacts. South Wales had the 2nd worst annual mean NO_2 levels (64 µg/m^3) across the entire UK according to UK government data in 2020, this was second to London (77 µg/m^3). South Wales exceeded the UK and EU legal limit (40 µg/m^3) by 160% (ClientEarth, 2022.). North Wales zone and Cardiff Urban Area also exceeded the national legal limit (with 44 and 42 µg/m^3 respectively) (ClientEarth, 2022). Levels of $PM_{2.5}$ also exceeded the recommended WHO guidelines. According to IQAir's 2019 World Air Quality Report, four out of ten Welsh locations with available data exceeded WHO's recommended limit of 10 µg/m^3 annually. In 2019, some of the most polluted locations were the town of Chepstow (12.6 µg/m^3); followed by major cities Cardiff (11.5 µg/m^3), Swansea (11.2 µg/m^3) and the town of Port Talbot (10.3 µg/m^3) (IQAir, 2019). WHO reduced the recommended annual concentration of $PM_{2.5}$ from 10 µg/m^3 to 5 µg/m^3, of PM_{10} from 20 µg/m^3 to 15 µg/m^3 and of NO_2 from 40 µg/m^3 to just 10 µg/m^3 in 2021 (WHO, 2021). New air pollution guidelines recommending lower levels of pollutants were due to increasing evidence indicating serious health implications of high pollutant levels (WHO, 2021).

Air pollution has negative consequences on various aspects of health. In 2017, air pollution exposure contributed to 1,400 premature deaths (at typical ages) in Wales (Welsh Government, 2019a). The most deprived parts of Wales have higher air pollution levels (Brunt *et al.,* 2016) and decreased life expectancy compared to less deprived areas (Currie *et al.,* 2021). Women and men, respectively live around six to seven years less compared to those in the least deprived areas (Currie *et al.,* 2021). Moreover, individuals in deprived areas are at higher risk of mental illness (Knifton & Inglis, 2020). Therefore, consideration of demographic variables such as deprivation is important when investigating the effects of air pollution on mental health. Overall, air pollution has been shown to have a negative impact on health and well-being as well as contributing to environmental health inequalities.

Previous research as stated above, has shown how demographic variables could influence the effects of air pollution on mental health. Therefore, descriptive statistics (age, sex, pollution levels, rural/city classification, and deprivation) will be generated for the general population and individuals with psychotic disorders. The purpose of this analyses is to create a baseline understanding on the distribution of mental health issues in different subgroups of the population. As previously highlighted in the introduction, there is little previous research in this area in Europe (Maconick *et al*., 2021). The purpose of this pilot study was to also connect a specifically identified mental health cohort to study within the confines of SAIL. The mental health cohort chosen was individuals with schizophrenia and other psychotic disorders (OPD). This was based on the outcome of the systematic review. Since, evidence detailed in Chapter 2 indicated that psychotic disorders were the most important mental health effect noted. Therefore, SAIL enables the investigation of the effects of air pollution on schizophrenia and OPD in Wales. To investigate associations between air pollution and a diagnosis of schizophrenia or OPD, exposure to historical air pollution will be linked for people living in Wales. A correlation test will be used to link air pollution data from 2016 and GP diagnoses of schizophrenia or OPD in the 3 years post exposure to determine if there is a potential association. Air pollution data is assigned to small areas in Wales. Small areas are Census geographies called Lower-layer Super Output Areas (LSOAs) (Office for National Statistics, 2023).

3.1.1 Aim:

To determine, the distribution of psychotic disorders in different subgroups of the population and if there is a correlation between PM_{10}, $PM_{2.5}$, or NO_x, and psychotic disorder diagnoses using SAIL data.

3.1.2 Hypothesis:

Air pollution is associated to increased risk of the onset of psychotic experiences, which is affected by demographic variables such as socioeconomic status.

3.1.3 Objectives:

To achieve the aim, the objectives are as follows:

1. Generate descriptive statistics using R software on age, sex, pollution levels in LSOA area, rural/urban classification, and deprivation from the general population and individuals with psychotic disorders.
2. Air pollution data from 2016 will be linked to GP diagnoses in the 3 years following using a correlation test.

3.2 Methods

3.2.1 Ethical Approval

Ethical approval was required for the use of population-based data such as mental health diagnoses available from the SAIL Databank. All proposals to use SAIL data are reviewed by an independent Information Governance Review Panel (IGRP). To access the data from SAIL, approval must be given by the IGRP. This organisation considers applications which describe project scoping to ensure proper and appropriate use of SAIL data. If access is approved, it is gained through a privacy-protecting safe haven and remote access system; termed SAIL Gateway (Mizen *et al.,* 2020). In **Figure 3.1** below the ethical approval process is summarised.

To gain ethical approval to access SAIL, an initial application was submitted as part of the process. The application contained a project summary, the plan to resource the project and the proposed analysis start date. In a meeting with JL the project requirements from SAIL were discussed. Therefore, a mutual understanding of the objectives and timeline of the project could be gained to proceed with ethical approval. This process allowed a scoping document with the associated costs to be made by the data scientist to aid in gaining ethical approval.

The next stage was the submission of the application (on the 15th December 2021) for internal IGRP review by members of the SAIL team. Amendments to the application were required such as further explanation of the datasets needed, and their importance. Consequently, the application was re-submitted for internal review on the 4th February 2022. Soon after, approval was granted by the internal review panel and the application progressed to the external review. Meanwhile, the safe researcher training course was taken and Curriculum Vitae (CV) submitted which are both required for SAIL access. The safe researcher training covers data security and personal responsibility, safe statistical outputs and how to use the environment efficiently as well as effectively. After approval by the IGRP, data provisioning took place so access could be gained to the SAIL gateway. The project number given was 1413. On approximately the 23rd March ethical approval was granted. Therefore, access to the SAIL gateway was authorised.

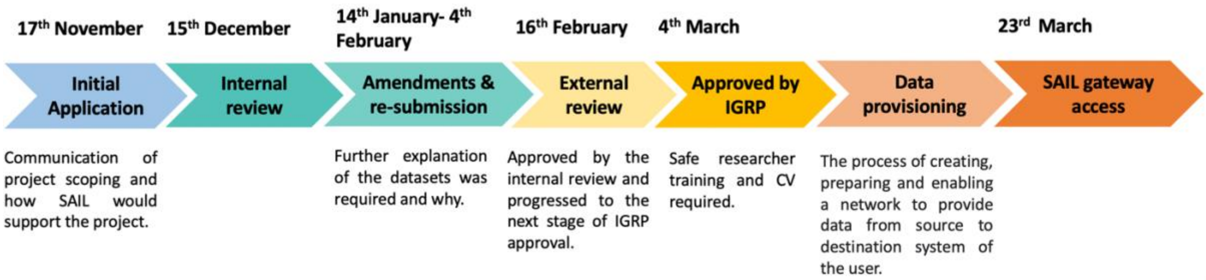

Figure 3.1- Ethical approval timeline with approximate dates of important milestones in the process.

3.2.2 Background

Data from approximately 2-million people living in a Welsh LSOA was used. Initially, descriptive statistics were generated on the age, sex, pollution levels in LSOA areas, rural/city residence, and socioeconomic position of the population and those with psychotic disorders. Then retrospective air pollution data from 2016 will be linked to the onset of psychotic disorders from 1st July 2016 until 30st June 2019. This study period was chosen to avoid covid periods (April 2019-December 2020) since there was a lot of disruption to GP services and patients reported difficulty accessing treatment (Healthwatch, 2021). The routinely collected data held in the SAIL Databank was used to answer the research questions:

1. What are the differences in terms of age, sex, pollution levels in LSOA areas, rural/city residence, and deprivation of the whole population compared to individuals with schizophrenia or other psychotic disorders?
2. Is the onset of psychotic disorders positively associated with increasing air pollution levels?

3.2.3 Setting

SAIL contains population data from individuals in Wales who are registered with a SAIL providing GP.

3.2.4 Participants

The criteria for eligible participants were:

- Registered with a Welsh GP between 1st July 2016 to 30th June 2019 (full 3-year follow-up).
- Same residence address between 1st July 2016 to 30th June 2019 to accurately assign exposure levels of pollutants from 2016 to participants.
- No restrictions on age, sex, and environment within the context of the population studied.

3.2.5 Data Linkage

The SAIL databank is a Trusted Research Environment containing anonymised environment and health data. This allows consistent data linkages at the individual and household level for the population of Wales. The purpose of the platform was to overcome data sharing issues such as protecting patients' privacy and facilitate investigating what impacts health. Initially to provide more detailed patient data, demographic information from the Welsh Demographic Service (WDS) was matched to the individuals in SAIL (GP dataset) (> 99.9%) (Lyons *et al.,* 2009). In the core SAIL datasets health and administrative data are routinely collected and available. The core datasets include: an anonymised linkable population register; mortality, inpatient, outpatient, and emergency department data as well as primary care data in Wales.

SAIL uses a 'split-file' anonymisation process (Lyons *et al.,* 2009). The file is split into two parts:

1) Identifiable name and address data.
2) The clinical or environmental non-identifiable data (Rodgers *et al.,* 2012).

A system linking field is added so data may be later re-joined within SAIL. Part 1 goes to a trusted third party, where the identifiers are replaced with a unique anonymous linking field (ALF) per person, or a Residential Anonymous Linking Field (RALF) for each residence. Part 2 of the dataset is sent straight to SAIL where the clinical or environment data are re-joined using the system linking field.

The Welsh Demographic Service Dataset (WDSD) contains administrative information and historic addresses for the population of Wales who are registered to a GP. This enables, alongside residential linkages, to allocate accurate exposure to individuals creating high spatial resolution air pollution data (Mizen *et al.,* 2018). Air pollution estimates in 2016 were linked to the home addresses of individuals from 1st July 2016 to 30th June 2019. The Welsh Longitudinal General Practice (WLGP) dataset was used to identify schizophrenia and other psychotic disorders diagnoses within the study period. This was completed by JL.

3.2.6 Quantifiable Variables

The mental health outcome, environmental exposures and demographic variables are defined in **Table 3.1**. Further explanation and description of these variables is below.

Mental Health Outcome

The mental health outcome was the onset of schizophrenia and other psychotic disorders. Since, evidence from the systematic review indicated these conditions were negatively affected by air pollution. The mental health data came from first GP diagnoses of these conditions from 1st July 2016 until 30st June 2019. Individuals who had a prior schizophrenia or other psychotic disorder diagnosis before the study start date were excluded.

Environmental exposure

The environmental exposure investigated was air pollution. Exposure to the main pollutants of concern $PM_{2.5}$, PM_{10} and NO_x in 2016 were downloaded from Lle- geo-portal for each LSOA in Wales. The effects of exposure to these pollutants in 2016 was investigated in the following three years (1st July 2016 until 30st June 2019).

Demographic Variables

In the descriptive statistics, age, sex, deprivation, and the environment people live in (rural or urban) were the demographic variables considered. Mental health and air pollution levels have been shown to be affected by these variables. Therefore, it is predicted that these variables could affect any potential association between air pollution and mental health.

Mental health ratings are predicted by sex, age, and socioeconomic status (Businelle *et al.,* 2014). Sex differences consistently found in research were women reported later age of onset than men of schizophrenia (Riecher-Rössler *et al.,* 2018). However, sex differences in incidence and symptomatology were less consistently reported (Riecher-Rössler *et al.,* 2018). In addition, the most common age of onset of mental disorders is in adolescents (14-25) (Solmi et al., 2021). Epidemiological studies have also shown links between growing up and living in cities with considerably higher schizophrenia risk (Gruebner *et al.,* 2017). In more deprived and urban areas research has found a higher prevalence and incidence of severe mental illness (schizophrenia and bipolar) (Lee *et al.,* 2020). This could be because air pollution concentrations were highest in the 'most' deprived and urban areas (Brunt *et al.,* 2016). The pollutants found at high levels in urban areas are NO_2 and CO, PM exposure is diverse, and ozone levels are often higher in rural areas (Blake & Wentworth, 2023). Those most vulnerable to the effects of air pollution are the elderly and children (Manisalidis *et al.,* 2020).

Therefore, overall, the relationship between these demographic variables and air pollution as well as mental health is complex. However, it is important to consider these variables to gain a more comprehensive understanding of their potential impacts on any association between air pollution and mental health. Therefore, in this study, descriptive statistics on age, sex, deprivation, and urban/rural classification were collected.

Table 3.1- The quantifiable variables in terms of outcome, exposure, and confounders.

Variable(s)	**Definition**	**Justification**
Outcome (Y-variable)	All individuals with new diagnoses of **schizophrenia and other psychotic disorders**.	This was the most noted mental health effect from the systematic review.
Exposure (X-variable)	Air pollution levels for **PM_{10}, $PM_{2.5}$** and **NO_x** from 2016.	These were the main pollutants of concern shown in the systematic review which is further supported by WHO.
Demographic	**Age**- mean and interquartile range. **Sex**- male/female. **Deprivation**- refers to wider problems caused by a lack of resources and opportunities. **Urban/rural classification** of the LSOA participants reside in.	Research shown in the paragraph above implies air pollution and mental health could be influenced by these variables. Generating descriptive statistics will therefore aid in understanding if this is also the case for the SAIL data. In addition, to helping understand if these variables could be confounders in any potential associations between air pollution and mental health.

3.2.7 Data Sources

The variables used in this study were from three datasets already available in the SAIL databank [Welsh Longitudinal General Practice (WLGP), Welsh Demographic Service (WDS), and Welsh Index of Multiple Deprivation (WIMD)]. As well as two additional datasets, air pollution from an internet platform and urban/rural classification from the Office for National Statistics (ONS). A description of the variables in this study are summarised in **Table 3.2** below.

Air Pollution

Air pollution data was downloaded from the internet platform Lle- geo-portal for Wales. This dataset is derived from UK wide Defra air pollution dataset. The Lle portal was developed in partnership between Welsh Government and Natural Resources Wales. It serves as a hub for data and information covering a wide spectrum of topics, but primarily around the environment. For this study, AM aggregated the levels of, PM_{10}, $PM_{2.5}$ and NO_x in 2016 from 10 km^2 grids to the LSOA level.

Welsh Longitudinal General Practise (WLGP)

The WLGP dataset contains individual-level health data including Read codes for all diagnoses, symptoms and treatments recorded for each person. A Read code is a coded thesaurus of clinical terms. In the NHS, Read codes have been used since 1985 and provide a standardised vocabulary for clinicians to record patient results across primary and secondary care (NHS Digital, 2022). The code lists used for schizophrenia and other psychotic disorders were taken from the SAIL Databank concept library:

- Schizophrenia-related disorders that include schizophrenia, schizotypal and delusional disorders: https://conceptlibrary.saildatabank.com/phenotypes/PH939/version/1957/detail/
- Other psychotic disorders were additionally mapped to ICD-10 codes for acute and transient psychotic disorders (F23), depressive episodes/disorders with psychotic symptoms (F32.3 and F33.3): https://conceptlibrary.saildatabank.com/phenotypes/PH938/version/1955/detail/

JL excluded individuals who had a prior schizophrenia or other psychosis diagnosis before the study start date (1st July 2016) to investigate the onset of these conditions.

Welsh Demographic Service (WDS)

The WDS is a population register that includes anonymised home addresses provided by patients registered with a Welsh GP. The residence of participants and if they move home is vital when calculating air pollution exposure (Mizen *et al.,* 2018). The WDS dataset, allowed the inclusion of individuals who continuously lived within the same LSOA for the study period. Therefore, air pollution data provided could be matched to the LSOA of the participants' residence.

Welsh Index of Multiple Deprivation (WIMD)

The WIMD data set is the Welsh Government's official measure of relative deprivation for LSOAs (Welsh Government, 2019b). WIMD identifies areas with the highest concentrations of eight different types of deprivation: income, employment, health, education, housing, access to services, community safety and physical environment (Welsh Government, 2022). All small areas in Wales are ranked from 1 (most deprived) to 1,909 (least deprived) (Welsh Government, 2019b). One area has a higher deprivation rank than another if the proportion of people living there who are classed as deprived is higher. It is a National Statistic produced by statisticians at the Welsh Government. The full index is updated every 4 to 5 years and the most recent index was published in 2019 (Welsh Government, 2019b). In this study the 2019 WIMD dataset was used.

Rural/urban Classification

The Rural Urban Classification is used to distinguish rural and urban areas from official government statistics (Office for National Statistics (ONS), 2016). In the classification system, output areas are defined as 'urban' if they have a population of 10,000 or more, while all remaining areas are defined as 'rural' (ONS, 2016). Those described as "in a sparse setting" reflect where the wider area is remotely populated (ONS, 2016). The urban and rural domains are subdivided into six broad settlement types:

- Rural town and fringe
- Rural village and dispersed in a sparse setting
- Rural town and fringe in a sparse setting
- Rural village and dispersed
- Urban city and town
- Urban city and town in a sparse setting

In the descriptive statistics the four subcategories 'rural town and fringe', 'rural village and dispersed in a sparse setting', 'rural town and fringe in a sparse setting' as well as 'rural village and dispersed' were all classified as 'rural and fringe' in the descriptive statistics. The two subcategories 'urban city and town' including 'urban city and town in a sparse setting' were classified together as city and town in the descriptive statistics.

Table 3.2- Provincial data available for each indicator.

Dataset name	**Data Source**	**Derived Variables**	**Coverage**
Air pollution	From an outside source: Lle- geo-portal for Wales.	The levels of PM_{10}, $PM_{2.5}$ and NO_x.	For each LSOA in Wales (n=1909).
Welsh Longitudinal General Practice (WLGP)	Primary care records recorded by GP.	Schizophrenia related disorders and other psychotic disorders.	~80% of GP practices in Wales.
Welsh Demographic Service (WDS)	NHS Wales Informatics Service	Age, sex, week of birth, multiple move in and out of home dates.	Total population of Wales registered with a General Practitioner, free at the point of service in the UK.
Welsh Index of Multiple Deprivation (WIMD)	Welsh government.	Relative deprivation from five (least deprived) to one (most deprived).	In 5 quintiles (5 equal groups of the population) from 2019 at the LSOA level.
Rural/urban Classification	From outside source: Office for National Statistics.	Urban or rural.	For each LSOA in Wales (n=1909).

3.2.8 Statistical Analysis

All analyses were conducted in R version 4.1.3 within the privacy protecting secure SAIL Databank environment. Data wrangling using the package dplyr was used to generate summary statistics and perform correlations. This process involved using code to select, transform, and map "raw data" into another format. The code used is in **Appendix A**. Section **A.1** in the appendices shows the code to install the package and cohort. The purpose of which was to make the data more appropriate and valuable for analysis.

Descriptive Statistics

Descriptive statistics were generated with code for the whole population (**Appendix A.2**) and for those with schizophrenia or other psychotic disorders (**Appendix A.3**). The descriptive statistics produced were:

- **Sex** (male/female)
- **Age** (mean, median, IQR)
- **Concentration of NO_x, PM_{10} and $PM_{2.5}$** (mean, minimum, median, maximum)
- **Rural urban classification** (rural and fringe/city and town)
- **Deprivation level** from one the most deprived to five the least deprived.

The code used to generate this data in SAIL are in **section A.2 and A.3 in the appendix**.

Correlation

In statistical terms, correlation is a bi-variate analysis that measures the strength of association between two variables and the direction of the relationship (Magiya, 2019). The correlation coefficient, denoted by r, measures the degree of the association (Schober *et al.*, 2018). However, correlation coefficients do not communicate information about whether one variable moves in response to another (Schober *et al.*, 2018). In terms of the strength and direction of the relationship, the value of the correlation coefficient varies between +1 and -1. A value of ± 1 indicates a perfect degree of association between the two variables. As the correlation coefficient value goes towards 0, the relationship between the two variables becomes weaker (Magiya, 2019). The direction of the relationship is indicated by the sign of the coefficient (+ or -). **Table 3.3** contains further information on different types of correlations and their meaning.

Table 3.3- Different types of correlations and their meaning.

Correlation coefficient value	**Correlation type**	**Meaning**
+1	Perfect positive correlation	When one variable increases as the other increases.
0	Zero correlation	There is no relationship between the variables (Schober *et al.*, 2018).
-1	Perfect negative correlation	When one variable changes, the other variable changes in the opposite direction.

Choosing a Correlation Test

There are different correlation tests that can be used depending on the type of data. Each test has assumed criteria that the data must meet. Two commonly used correlation tests are Pearson's R and Spearman's Rho (Bhandari, 2021). **Table 3.4** details the assumed criteria of the tests based on the type of relationship, levels of measurement, data distribution and if they are affected by outliers. Levels of measurement is defined as how precisely variables are recorded. The definition of some of the terms used to describe the levels of measurement are:

- **Quantitative:** the value of data in the form of counts or numbers where each data set has a unique numerical value.
- **Interval:** the data can be categorized, ranked, and evenly spaced such as test scores (Bhandari, 2021).
- **Ratio:** the data can be categorized, ranked, evenly spaced, and has a natural zero such as height or age (Bhandari, 2021).
- **Ordinal:** classified into categories within a variable that have a natural rank order (Bhandari, 2021). However, the distances between the categories are uneven or unknown (Bhandari, 2021). For example, satisfaction rating ("extremely dislike", "dislike", "neutral", "like", "extremely like").

Table 3.4- Correlation tests and their criteria.

Correlation Coefficient	**Pearson's r**	**Spearman's rho**
Type of Relationship	Linear- straight-line relationship	Non-linear
Levels of Measurment	Two quantitative (interval or ratio) variables	Two ordinal, or quantitative variables
Data Distribution	Both variables have normal distribution (symmetrical and shaped like a bell).	Any distribution *e.g.,* skewed
Affected by Outliers	Yes- may exaggerate or dampen the strength of relationship.	No

Therefore, to decide on the correlation test to use, the data was tested for normal or any other distribution in R by creating histograms and boxplots (Korstanje, 2019). A histogram with roughly a "bell-shape" shows data that is normally distributed (Korstanje, 2019). Histograms with data that is skewed to the left or right exhibits a dataset that is not normally distributed. For boxplots, when the median is in the middle of the box, and the whiskers are about the same length on both sides of the box, then the distribution is symmetric (MacLeod, 2019). When the median is closer to the bottom of the box, and if the whisker is shorter on the lower end of the box, then the distribution is positively skewed (skewed right) (MacLeod, 2019). When the median is closer to the top of the box, and if the whisker is shorter on the upper end of the box, then the distribution is negatively skewed (skewed left) (MacLeod, 2019). An outlier is an observation that is numerically distant from the rest of the data and is located outside the whiskers of a box plot (MacLeod, 2019). Boxplots and histograms were created in R to find the distribution of the variables that would be used in the correlation. The code used is in **7.1.5 in the appendix**. The boxplots and histograms in **Figure 3.2** demonstrated that:

- NO_x means- were right skewed with outliers (**Figure 3.2: A and 3.2: B**).
- $PM_{2.5}$ means- were normally distributed with outliers (**Figure 3.2: C and 3.2: D**).
- PM_{10} means- were normally distributed with outliers (**Figure 3.2: E and 3.2: F**).
- Percentage of people with schizophrenia or OPD in NO_x concentrations ranging from 3-54 $\mu g/m^3$- skewed left with outliers.

- Percentage of people with schizophrenia or OPD in $PM_{2.5}$ concentrations ranging from 4-10 μg/m^3- skewed right with no outliers.
- Percentage of people with schizophrenia or OPD in PM_{10} concentrations ranging from 7-16 μg/m^3- skewed left with an outlier.

The boxplots and histograms for the percentage of schizophrenia and OPD diagnoses could not be requested out of SAIL due to the data containing groups of less than five.

Therefore, the correlation test chosen to use in R was Spearman's rho because:

- Robust when (outliers) are present (all pollutants had outliers).
- PM_{10} and $PM_{2.5}$ were normally distributed however both variables had outliers.
- NO_x was not normally distributed.
- Percentage of people with schizophrenia or OPD data for NO_X, $PM_{2.5}$ and PM_{10} were skewed.
- The air pollutant concentrations and percent with a schizophrenia/OPD are quantitative.

To use the correlation test function in R both the pollutant concentrations (x-variable) and the frequency of people with schizophrenia or OPD (y-variable) had to be transformed into a different format. The x-variable needed to be defined as numeric integers of the pollutant in R. The y-variable was transformed into the percentage of people with a schizophrenia or OPD in the population at each pollutant value. Initially a frequency table was made of the number of people with schizophrenia or OPD at the different concentrations of the chosen air pollutant. This table was converted to a data frame. The column names were changed to 'concentration', 'na', 'mental health frequency.' In the 'na' column only the values that were true were needed as these met the criteria set (people with schizophrenia or OPD). Similarly, as previously described but with the whole population a frequency table was made of the number of people in the population per pollutant. The table was converted to a data frame and the columns changed to 'concentration', 'na', 'population frequency.' The two data frames, schizophrenia or OPD frequency and population frequency, were merged using the column 'concentration.' This enabled the calculation of the percentage of people with schizophrenia or OPD per pollutant concentration by dividing those with a schizophrenia or OPD by the population size at the different pollutant values. The concentration values were defined as factors in R. Therefore, the values were changed to numeric so the concentration values could be used in the correlation and accurately plotted. This process was done separately for each pollutant. The 'x' and 'y' variables for the correlation were:

- x= integers of the concentrations of air pollutants ($PM_{2.5}$, PM_{10} and NO_x)

- y= the percentage of people with schizophrenia or OPD

The spearman's correlation test and correlation coefficient were computed using the code:

- **cor.test** (x, y, method = "spearman")

The output from the correlation test were:

- **S** is the value of the test statistic.
- ***p*-value** is the significance level of the test statistic.
- **alternative hypothesis** is a character string describing the alternative hypothesis (true rho is not equal to 0).
- **sample estimates** are the correlation coefficient. For Spearman correlation coefficient it's named as **rho**.

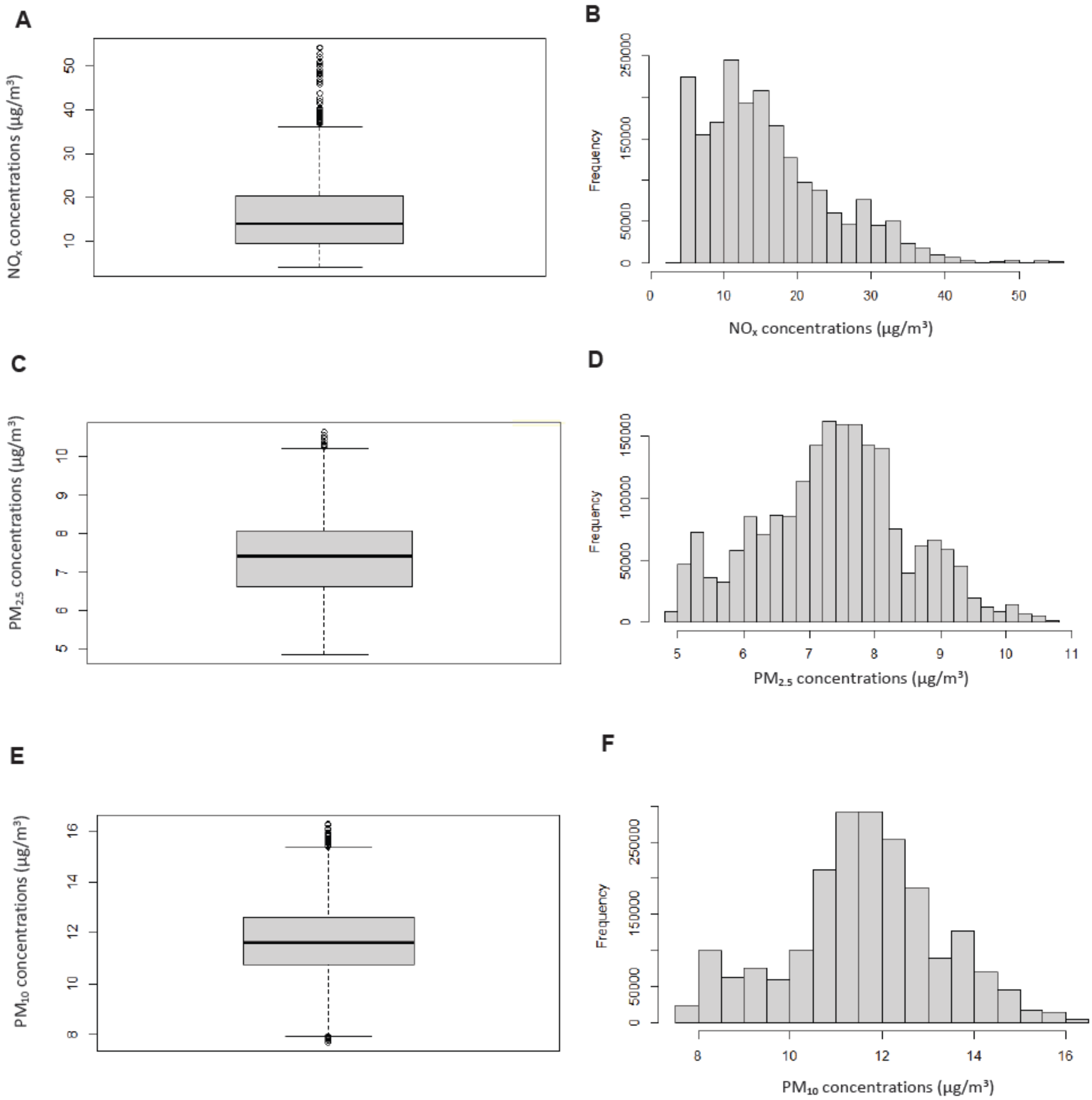

Figure 3.2- Boxplots and histogram of the NO_x (A and B), $PM_{2.5}$ (C and D), and PM_{10} (E and F) means created in R. **A)** In the **NO_x boxplot,** the median is closer to the bottom of the boxplot and the whisker is shorter on the lower end of the box, then the distribution is positively skewed (skewed right). There are also outliers on the top of the box. **B)** The **NO_x histogram** is skewed to the right as the peak of the graph lies to the left side of the centre. **C)** In the **$PM_{2.5}$ boxplot**, the median is in the middle of the box, and the whiskers are about the same length on both sides of the box, so distribution is symmetric. There are also outliers on the top of the box. **D)** The **$PM_{2.5}$ histogram** is roughly a "bell-shape" which shows that the data is normally distributed. **E)** In the **PM_{10} boxplot**, the median is in the middle of the box, and the whiskers are about the same length on both sides of the box, so distribution is symmetric. There are also outliers on the top and bottom of the box. **F)** The **PM_{10} histogram** is roughly a "bell-shape" so the data is normally distributed.

The terminology from the output of the correlation test will be briefly described and recapped in **Table 3.5** below.

Table 3.5- Terminology in the correlation test output.

Terminology	**Definition**
Test statistic	Assesses how consistent your sample data are with the null hypothesis (Gravetter & Wallnau, 2014). More extreme values indicate larger differences between your sample data and the null hypothesis (Gravetter & Wallnau, 2014). This value helps to reject the null hypothesis by showing incompatibility with the null hypothesis, and to calculate the *p*-value (Gravetter & Wallnau, 2014).
***p*-value and significance level**	Assuming that the null hypothesis is true, the *p*-value is the probability of obtaining test results that are at least as extreme as the observed results (Dahiru, 2008). To draw conclusions concerning the null hypothesis, the *p*-value is compared to a selected significance level (α) (Dahiru, 2008). The significant level is the probability of rejecting the null hypothesis given that the null hypothesis is true (Dahiru, 2008). Results are considered statistically significant when the *p*-value allows the null hypothesis to be rejected, which occurs for *p*-values less than or equal to the significance level, or: $p \leq \alpha$. Alpha is usually defined as 0.05 (Dahiru, 2008).
Null hypothesis (H_0)	There's **no effect** in the population (Turney, 2022).
Alternative hypothesis (H_A)	There's an **effect** in the population (Turney, 2022).
Correlation coefficient	Measures the degree of association (Schober *et al*., 2018)

The relationship between x and y can be plotted in R using a simple scatter graph. Section **A.6** in the appendix contains the code used in SAIL to complete the correlations per pollutant. Section **A.6.1** has the correlations for NO_x, **A.6.2** for $PM_{2.5}$ and **A.6.3** for PM_{10}.

Once the descriptive statistics and correlation data were generated, the documents needed were requested out of SAIL gateway and had to be approved for use. Data that represents individuals or groups of less than five was not approved out of the SAIL gateway.

3.3 Results

3.3.1 Descriptive Statistics

In total 2,021,810 individuals were analysed who were registered with a Welsh GP and stayed in the same home address between the 1st July 2016 to 30th June 2019. In the same time period, 0.088% (1,784) had a diagnosis of schizophrenia or other psychotic disorders (OPD) in this population. Out of the 1784 individuals, 50.4% (899) had a diagnosis of schizophrenia only, 43.5% (776) had a diagnose of OPD only and 6.1% (109) were diagnosed with both conditions.

Table 3.6- Description of the number of participants.

Participants	**Number**	**Percentage of all participants (%)**
Total population	2,021,810	(100)
Schizophrenia only	899	(0.044)
OPD only	776	(0.038)
Schizophrenia and OPD	109	(0.0054)
Schizophrenia or OPD	1784	(0.088)

A description of the number of participants in the total population and the sub-groups is given in **Table 3.6 above**.

The characteristics of the whole population and those with schizophrenia or OPD are summarised in **Table 3.7** below. More participants (52.7%) were male compared to female (47.3%) in the schizophrenia/OPD cohort. The mean age of the participants in the whole population was 42.26 and 46.92 in the schizophrenia or OPD cohort. Upper and lower quartiles were also higher (28-65) in the schizophrenia/OPD cohort compared to the whole population (23-61). There were more people with schizophrenia or OPD in the areas classified as city and town (0.091%) compared to areas classified as rural and fringe (0.083%). The descriptive statistics showed there were more diagnoses of schizophrenia or OPD in the most deprived areas compared to the least deprived areas. For example, the percentage of schizophrenia/OPD diagnoses in the most deprived areas (WIMD 1) was more than double (0.13%) the percentage in the least deprived areas (WIMD 5) (0.06%). This is shown in **Figure 3.3** below.

Table 3.7- Characteristics of all participants and those with schizophrenia or OPD.

Characteristics	**All**	**Schizophrenia or OPD**	**Percent of all participants (%)**
Sex			
Male	1,014,575 (50.2%)	941 (52.7%)	0.093
Female	1,007,235 (49.8%)	843 (47.3%)	0.084
Age			
Mean	42.26	46.92	NA
Median	44	45	NA
IQR	23-61	28-65	NA
Environment			
Rural and fringe	596,594	494	0.083
City and town	1,425,216	1,290	0.091
WIMD			
1 (Most deprived)	413,529	519	0.13
2	411,408	408	0.099
3	393,140	298	0.0758
4	384,453	292	0.0760
5 (Least deprived)	419,280	267	0.06

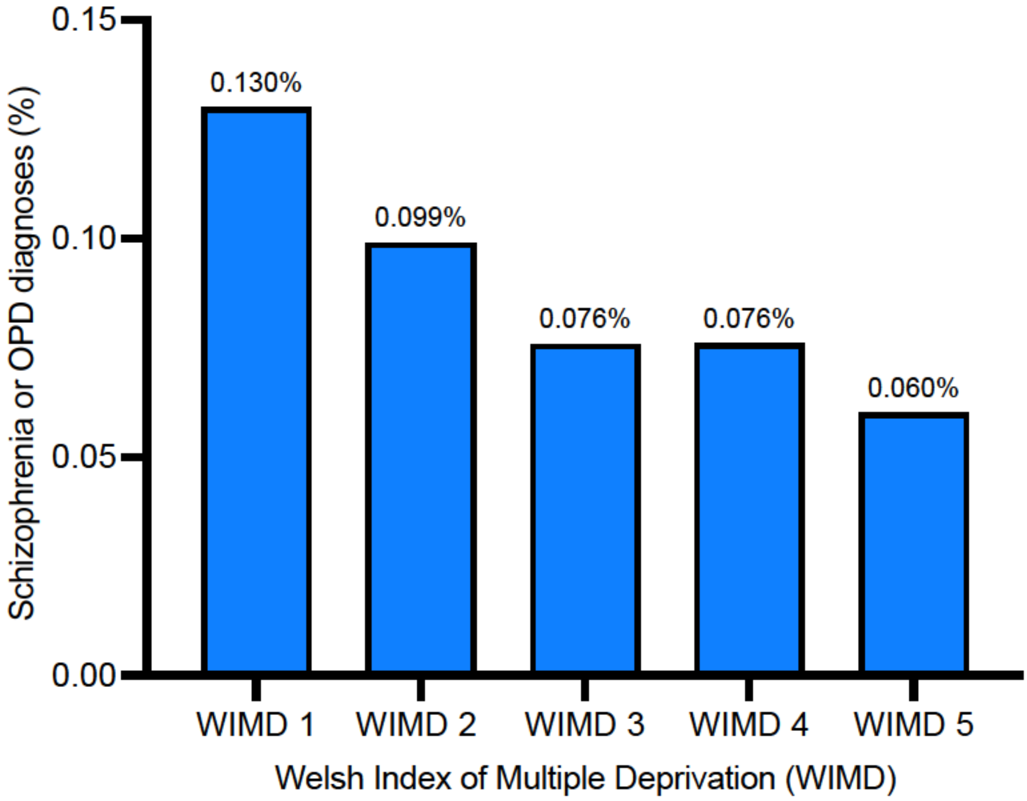

Figure 3.3- The percentage of people with schizophrenia or OPD at different levels of deprivation from most deprived (WIMD 1) to least deprived (WIMD 5).

The levels of the pollutants PM_{10}, $PM_{2.5}$ and NO_x were similar in the schizophrenia/OPD cohort and in all participants as shown in **Tables 3.8, 3.9** and **3.10** respectively.

For PM_{10}, the WHO recommended concentration was 20 µg/m^3 annually from 2005-2020. However, in 2021 the recommendation was lowered to 15 µg/m^3. The mean concentration of PM_{10} in 2016 in Wales was less than the recommended concentration in the whole population (11.60 µg/m^3) and the schizophrenia/OPD cohort (11.59 µg/m^3). The minimum and maximum concentrations of PM_{10} in both groups were 7.69 µg/m^3 and 16.31 µg/m^3. This is summarised in **Table 3.8** below.

Table 3.8- PM_{10} concentrations in all participants and those with schizophrenia or OPD.

PM_{10} (µg/m^3)	**All Participants**	**Participants with Schizophrenia or OPD**
Mean	11.60	11.59
Minimum	7.69	7.69
Median	11.65	11.64
Maximum	16.31	16.31

For $PM_{2.5}$, the WHO recommended concentration was 10 µg/m^3 annually in 2005-2020. However, in 2021 the recommendation was lowered to 5 µg/m^3. The mean concentration of $PM_{2.5}$ in 2016 in Wales was higher than the 2021 recommendation however lower than the previous recommendation. The mean value was 7.38 µg/m^3 in the whole population and 7.37 µg/m^3 in participants with schizophrenia or OPD. The minimum and maximum concentrations of $PM_{2.5}$ in both groups were 4.83 µg/m^3 and 10.64 µg/m^3. This is summarised in **Table 3.9** below.

Table 3.9- $PM_{2.5}$ concentrations in all participants and those with schizophrenia or OPD.

$PM_{2.5}$ (µg/m^3)	**All Participants**	**Participants with Schizophrenia or OPD**
Mean	7.38	7.37
Minimum	4.83	4.83
Median	7.41	7.42
Maximum	10.64	10.64

For NO_2, the WHO recommended concentration was 40 µg/m^3 annually in 2005-2020. However, in 2021 the recommendation was lowered to 10 µg/m^3. The mean concentration of NO_x in 2016 in Wales was 15.92 µg/m^3 in the whole population and 15.75 µg/m^3 in participants with schizophrenia or OPD. This was lower than the recommended pollutant concentration at the time but above the new 2021 recommendation. The minimum pollutant concentration was 3.96 µg/m^3 in the whole population and 4.02 µg/m^3 in the schizophrenia or OPD group. The maximum was 54.33 µg/m^3 in both groups. This is summarised in **Table 3.10** below.

Table 3.10- NO_x concentrations in all participants and those with schizophrenia or OPD.

NO_x (µg/m^3)	**All Participants**	**Participants with Schizophrenia or OPD**
Mean	15.92	15.75
Minimum	3.96	4.02
Median	14.16	14.32
Maximum	54.33	54.33

The code used to generate the air pollution data in R are shown in section **A.4** in the appendices.

3.3.2 Spearman's Rank Correlations (rho)

Data:

x= range of NO_x concentrations

y= percentage of people with schizophrenia or OPD

S = 21019, *p*-value = 0.621

alternative hypothesis: true rho is not equal to 0

sample estimates:

rho: -0.07241644

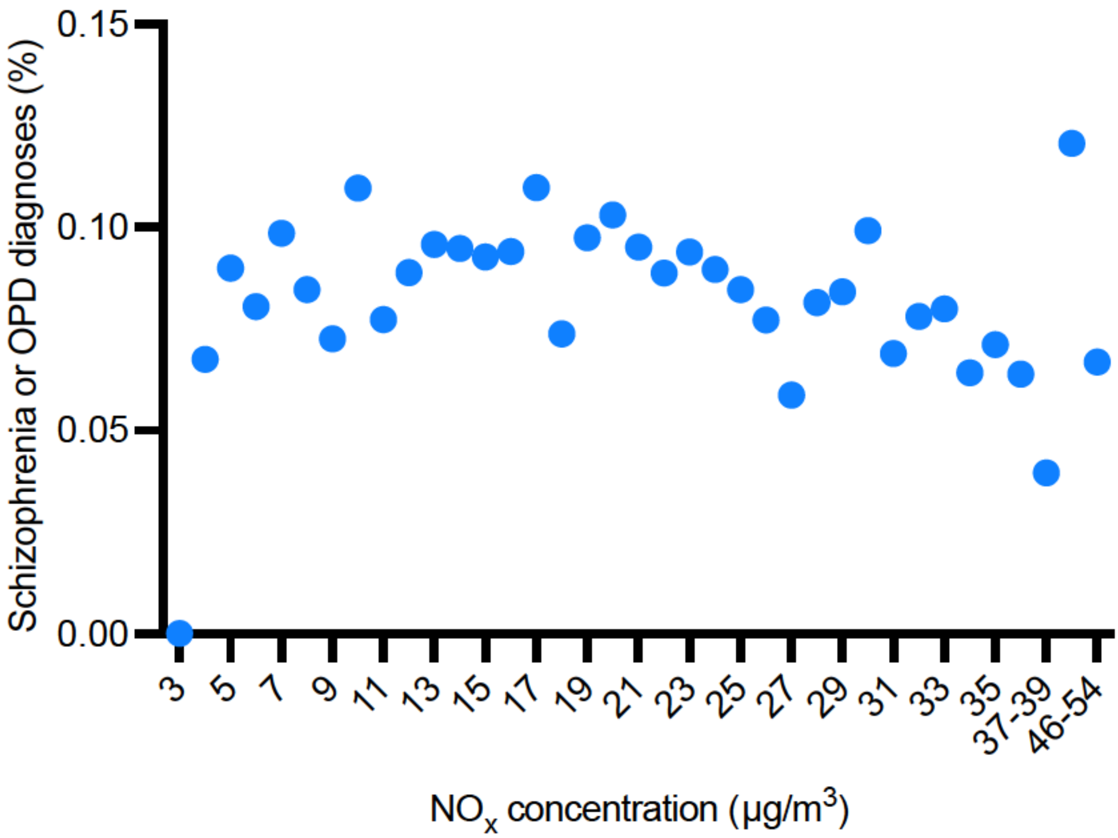

Figure 3.4- Correlation between NO_x concentrations from 3 to 46-54 and the percentage of people with schizophrenia or OPD. The individual pollutants from 37 to 54 contained numbers of people less than 5 so multiple concentrations were combined (37-39, 40-45 and 46-54). The data used to create the graph is in **Table B.1** in **Appendix B**.

No correlation was found between NO_x concentrations and the percentage of people with schizophrenia or OPD. Since the correlation coefficient (-0.072) was close to zero. The *p*-value is greater than 0.05 therefore the result is non-significant. Since, the *p*-value is 0.621 which means there is a 62% chance that a result occurred by random chance, given that the null hypothesis is true. Thus, a high *p*-value provides evidence for not rejecting the null hypothesis in favour of the alternative hypothesis. Since this indicates it is highly likely that the outcome could have occurred by chance. The code used to generate these results is in section **A.6.1**.

Data:

x= range of $PM_{2.5}$ concentrations

y= percentage of people with schizophrenia or OPD

S = 44, *p*-value = 0.6615

alternative hypothesis: true rho is not equal to 0

sample estimates:

rho: 0.2142857

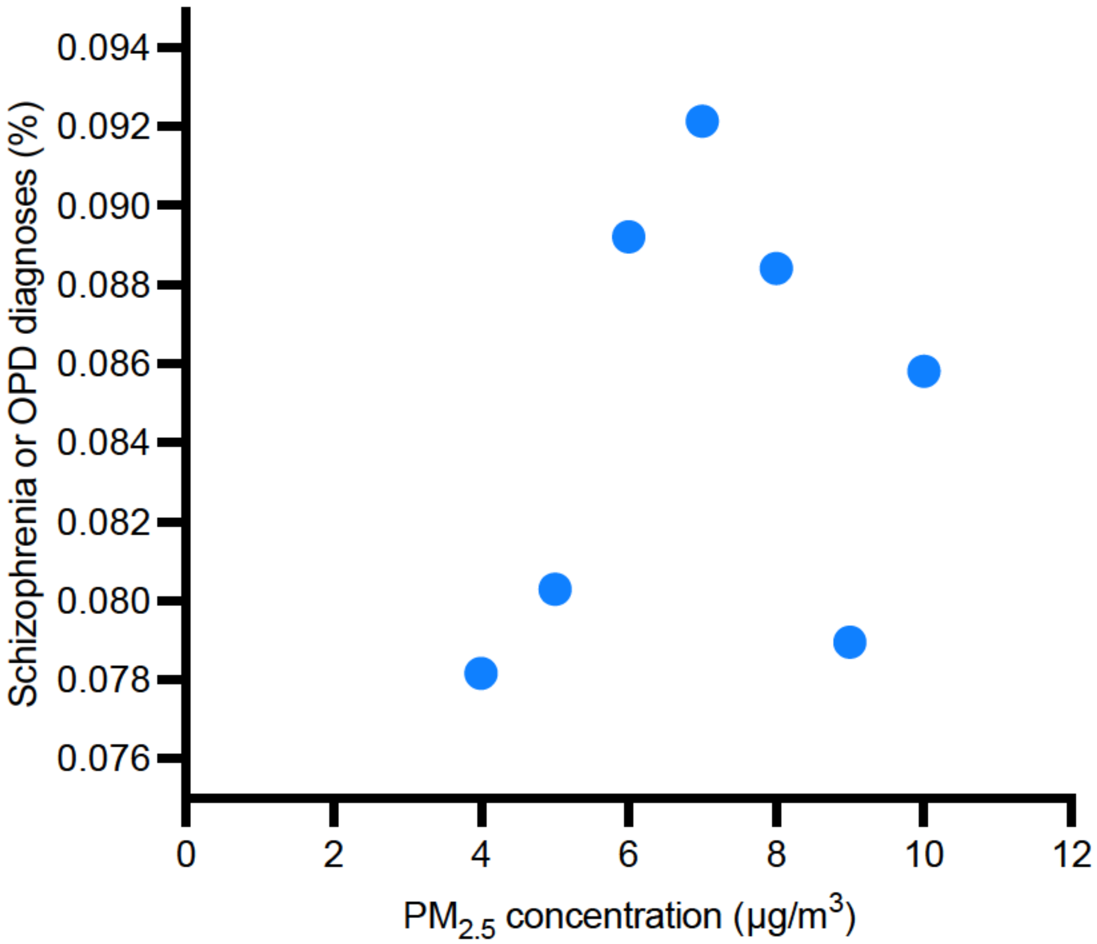

Figure 3.5- Correlation between $PM_{2.5}$ concentrations from 4 to 10 µg/m³ and the percentage of people with schizophrenia or OPD. The data used to create the graph is in **Table B.2** in **Appendix B**.

A weak positive correlation was found between $PM_{2.5}$ concentrations and the percentage of people with schizophrenia or OPD. Therefore, as $PM_{2.5}$ increased so did the percentage of people with a schizophrenia or OPD diagnosis. The *p*-value is bigger than 0.05 therefore the result is non-significant. Since, the *p*-value is 0.662 which means there is approximately a 66% chance that the result occurred by random chance, given that the null hypothesis is true. Thus, a high *p*-value provides evidence for not rejecting the null hypothesis in favour of the alternative hypothesis. Since it indicates that it is highly likely that the outcome could have occurred by chance. The code used to generate these results is in section **A.6.2**.

Data:

x= range of PM_{10} concentrations

y= percentage of people with schizophrenia or OPD

S = 224, *p*-value = 0.3128

alternative hypothesis: true rho is not equal to 0

sample estimates:

rho: -0.3575758

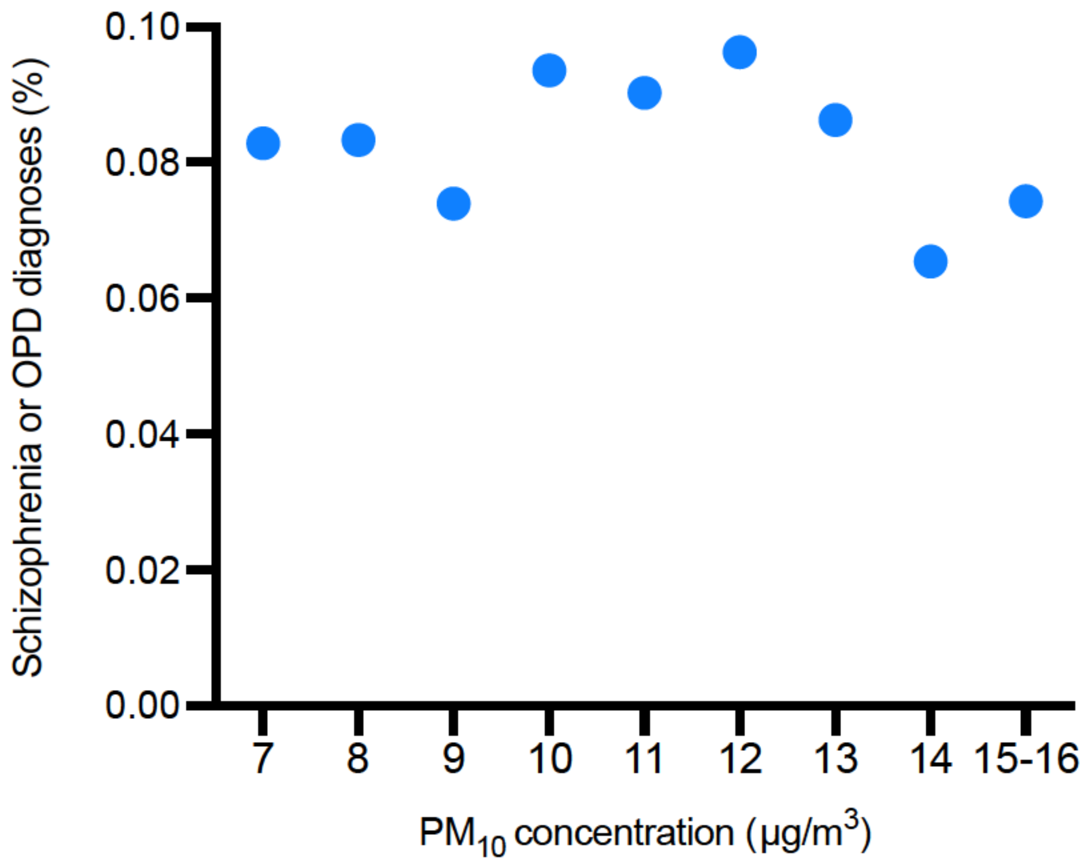

Figure 3.6- Correlation between $PM_{2.5}$ concentrations from 7 to 15-16 µg/m³ and the percentage of people with schizophrenia or OPD. The pollutant with a concentration of 16 contained a number of people less than 5 so the concentrations 15 and 16 were combined. The data used to create the graph is in **Table B.3** in **Appendix B**.

A weak negative correlation was found between PM_{10} concentrations and the percentage of people with schizophrenia or OPD. Therefore, as PM_{10} concentration increased the percentage of people with schizophrenia or OPD slightly decreased. The *p*-value is bigger than 0.05 therefore the result is non-significant. Since, the *p*-value is 0.313 which means there is approximately a 31% chance that the result occurred by random chance, given that the null hypothesis is true. Thus, a high *p*-value provides evidence for not rejecting the null hypothesis in favour of the alternative hypothesis. Since it indicates that it is highly likely that the outcome could have occurred by chance. The code used to generate these results is in section **A.6.3**.

3.4 Discussion

Previous research detailed in Chapter 1 was heterogenous in terms of the design, exposure, and outcome. Therefore, the purpose of the pilot study was to investigate if its results would support the evidence from the systematic review that PM_{10}, $PM_{2.5}$ and NO_2 were most hazardous to psychotic disorders. In addition, the objective of this study was to explore the prevalence of psychotic disorders in subgroups of the population to identify potential vulnerable groups.

Descriptive statistics

In this pilot study, the level of deprivation was shown to affect the percentage of individuals with a diagnosis of schizophrenia or OPD. Since there was a higher percentage of people with schizophrenia or OPD in more deprived areas. Deprivation in terms of income, employment, health, education, housing, access to services, community safety and physical environment was considered. The findings that there is a higher percentage of schizophrenia and OPD diagnoses in deprived areas is supported by the literature. A population-based linkage study which also used primary care data found prevalence and incidence of schizophrenia was higher in more deprived areas (Lee *et al.,* 2020). Deprivation has also been shown to be associated with increased mental health service use (Maconick *et al.*, 2021). Therefore, individuals in deprived areas could be more at risk of mental disorders (Bernardini *et al.,* 2019; Knifton & Inglis, 2020). This supports the hypothesis that demographic variables such as socioeconomic status could affect an association between air pollution and mental health. Whereas, the other demographic variables investigated, sex, age and rural or city residence, did not show much variation between the schizophrenia /OPD cohort and the whole population in this pilot study. Despite, findings which were emphasised in the introduction that individuals in urban areas are at higher risk of schizophrenia and other mental disorders (Gruebner *et al*., 2017; Lee *et al.,* 2020; Ventriglio *et al*., 2020).

Correlation

A positive correlation was found between $PM_{2.5}$ concentrations and percentage of people with a diagnosis of schizophrenia or OPD. This supported the hypothesis since, as the $PM_{2.5}$ concentration increased so did the percentage of people with a new diagnosis of schizophrenia or OPD. Therefore, higher concentrations of $PM_{2.5}$ were shown in this data to have a negative impact on schizophrenia and OPD. However, the correlation coefficient was non-significant (*p*-value= 0.6615). Antonsen *et al*. (2020) also found a slightly positive but non-significant association between long-term $PM_{2.5}$ exposure and future schizophrenia diagnoses. In contrast, a study found no association between schizophrenia and $PM_{2.5}$ (Li *et al.,* 2020). However, high concentrations of $PM_{2.5}$ were associated with increased hospital admissions for schizophrenia (Bai *et al.,* 2020). Additionally, increasing levels of $PM_{2.5}$ were significantly related to psychosis emergency department visits (Lee *et al.,* 2022). Previous annual exposure to $PM_{2.5}$ was significantly associated to adolescent psychotic experiences however this only explained 40% of the association in contrast to NO_2 and NO_x (Newbury *et al.,* 2019). Therefore, overall, a positive association between $PM_{2.5}$ and psychosis or schizophrenia has also been found by previous research.

No correlation was found between NO_x concentrations and the percentage of people with schizophrenia or OPD. This result did not support the hypothesis as NO_x was shown to not influence the onset of schizophrenia or psychosis. Only one article from the systematic review found no association between NO_2 and schizophrenia (Thilakaratne *et al.,* 2020). In contrast to findings in SAIL NO_2 was positively associated to psychotic disorders in ten studies. Previous annual exposure to NO_2 and NO_x was significantly associated to adolescent psychotic experiences which explained 60% of the association (Newbury *et al.,* 2019). Short-term increases in NO_2 were noted to be associated with hospital admissions for psychosis (Tong *et al.,* 2016; Lee *et al.,* 2022). Long-term exposure to NO_2 was also significantly positively associated to future schizophrenia diagnoses (Horsdal *et al.,* 2019; Antonsen *et al.,* 2020). In addition, higher concentrations of NO_2 were associated to rising risk for schizophrenia visits (Liang *et al.,* 019). Positive associations to schizophrenia hospital admissions were also found in numerous studies (Duan *et al.,* 2018; Bai *et al.,* 2019; Li *et al.,* 2020; Lu *et al.,* 2020). Despite, finding no correlation between NO_x concentrations and the percentage of people with schizophrenia or OPD most studies from the systematic review found positive associations.

A negative correlation was found between PM_{10} concentrations and percentage of people with a diagnosis of schizophrenia or OPD. This did not support the hypothesis because as PM_{10} concentrations increased the percentage of people with schizophrenia or OPD slightly decreased. Therefore, in this pilot study higher PM_{10} concentrations were not negatively impacting psychotic disorders. Newbury and colleagues also did not find an association between PM_{10} and adolescent psychotic experiences. However, in another study, PM_{10} was associated with increased risk of daily psychosis hospital admissions (Tong *et al.,* 2016). Furthermore, multiple studies found increasing concentrations of PM_{10} were associated to schizophrenia hospital admissions (Duan *et al.,* 2018: Liang *et al.,* 2019; Bai *et al.,* 2020). Despite, the varied associations found between psychotic disorders and PM_{10}, more research found PM_{10} had a negative impact in contrast to the data from SAIL.

Overall, a positive correlation was found between $PM_{2.5}$ concentrations and the onset of schizophrenia or OPD. Deprivation level was the only variable which appeared to affect the percentage of individuals with a diagnosis of schizophrenia or OPD. Those in the deprived areas could be more at risk of having a schizophrenia or OPD diagnosis.

3.4.1 Limitations and Future Research

Some of the main limitations of the SAIL data used in this pilot study are listed and explained in **Table 3.11**. Acknowledging the limitations enables recommendations for future research as highlighted in **Table 3.11** below.

Table 3.11- Identifies and explains the limitations of the SAIL data as well as future recommendations.

Limitation	**Explanation**	**Future Recommendation**
Measuring individual pollution exposure	Accurately and reliably estimating air pollution exposure for participants is a common difficulty in air pollution studies (Hahad *et al.,* 2020). Since, participants may go to multiple different locations throughout the day such as work or school. The air pollution data in this study was not at the home address level but at the LOSA level (1,500 people approximately per LOSA).	Increase spatial resolution of air pollution data by measuring exposure at multiple locations such as work or school and residence.
Pollutant mixture and source	The source of pollutants that individuals are exposed to will differ depending on their locations and if they live in cities or rural locations (Blake & Wentworth, 2023). Therefore, the pollutant source could affect the mental health impacts due to differences in the pollutant mixture.	More research into which components of air pollution could be contributing to mental health disorders.
Small number of people with schizophrenia or OPD (only 0.088%) and the use of only GP data	This could limit the generalisability and reliability of the findings. Especially since at higher pollutant concentrations there were very few people (**Tables B.1, B.2 & B.3** in **Appendix B**). This was also seen by Lowe *et al.* (2020) and led to uncertainty around estimates at higher concentrations. Although, the use of	Future studies could include more subjects by collecting data from various mental health settings such as GP, inpatient and outpatient hospital records. This could

	GP data at the individual level did provide high resolution data.	increase the number of people and how representative the data was.
Current (2020 or 2021) data on air pollution and diagnoses not used.	As previously justified the 1st July 2016 until 30st June 2019 was the chosen study length to avoid covid periods. Since, during April 2019 to December 2020, GP access was difficult and disrupted (Healthwatch, 2021). A thematic analysis of 10,089 people reported difficulties booking appointments, appointment's not meeting people's needs and a lack of access to regular treatment and medication (Healthwatch, 2021).	The use of more up-to-date records where possible.
Not including bipolar in the mental health cohort	Since, the pilot study was building on data from the systematic review in which only one paper investigated bipolar. Whereas in the review there was more focus (13 articles) on schizophrenia and psychosis. However, in a clinical setting bipolar would be considered a psychotic disorder.	More research which investigates the potential effects of air pollution on bipolar.
Correlation which only involves two variables	More complex statistical modelling was beyond the scope of the project. However, the use of more complex techniques such as regression which relates a dependent variable to one or more independent variables is important for investigating the effects of air pollution on mental health (Crawford, 2006). Since, confounders are likely to affect the association such as: - **Deprivation**- descriptive statistics in this study found more than double the	Use of regression which allows the consideration of confounding variables such as deprivation.

	percent of people with schizophrenia or OPD in the most deprived compared to the least deprived areas. This is supported by research (Bernardini *et al.,* 2019; Reiss *et al.,* 2019; Knifton & Inglis, 2020). The simultaneous consideration of air pollution and deprivation is emphasised by Brunt et al. (2016) since air pollution exacerbated deprivation health associations. - **Lifestyle factors** *e.g.,* smoking status and alcohol consumption- individuals with mental health conditions are more likely to smoke (Smith *et al.,* 2014) and drink more between occasions (Bell & Britton, 2014).	

- The descriptive statistics and correlations explained in section 3.4 provides a basis for future work on other mental health conditions using SAIL.

4 General Discussion

The aim of this thesis was to determine, with consideration of demographic factors, if there was an association between air pollution, particularly PM, O_3, NO_2, SO_2, CO and reduced mental health as well as well-being. This was achieved by conducting a systematic review, and then using SAIL to link retrospective air pollution and mental health diagnoses. It was hypothesised that air pollution could have a negative impact on mental health and well-being, which was further confounded by socioeconomic factors.

The majority of the literature assessed within the systematic review supported the hypothesis that air pollution could have a negative impact on mental health and well-being. Notably, associations appeared to be strongest for increases in $PM_{2.5}$, PM_{10} or NO_2 and psychotic disorders compared to the other conditions reviewed (*i.e.*, anxiety and suicide related). The most noted negative effect was from NO_2 on psychotic disorders such as psychosis and schizophrenia which was found by ten studies. The negative outcomes were onset, as well as increased severity, and relapse in symptoms or readmission to hospital. Therefore, in the SAIL analysis, other psychotic disorders and schizophrenia GP records were correlated with $PM_{2.5}$, PM_{10} or NO_x. The hypothesis was supported since a weak positive correlation was found between $PM_{2.5}$ and the percentage of schizophrenia or OPD diagnoses. However, the hypothesis was disproved by NO_x and PM_{10} because there was no correlation and a weak negative correlation to psychotic disorders respectively. The hypothesis may not be supported because of SAIL data limitations such as a small number of psychotic diagnoses particularly at higher concentrations. This is shown in **Tables B.1, B.2, and B.3** in **Appendix B**. Moreover, a sample size which would enable clinically meaningful results was not calculated. As previously discussed in section 3.4.1 in **Table 3.11,** this was also seen in a study by Lowe *et al*. (2020) and caused uncertainty around the effect estimates. Therefore, the sample size may not have been large enough to demonstrate clinical effects.

In the systematic review, three studies demonstrated significant positive associations between $PM_{2.5}$ and schizophrenia hospitalisation (Bai *et al.,* 2020) as well as psychotic experiences (Newbury *et al.,* 2019; Lee *et al.,* 2022). Other negative impacts on schizophrenia linked to $PM_{2.5}$ were increased severity (Eguchi *et al.,* 2018) and relapse (Gao *et al.,* 2021; Ji *et al.,* 2021; Wei *et al.,* 2021). Contrastingly, the association between $PM_{2.5}$ and schizophrenia hospitalisations were less clear or consistent and there was little evidence after adjustment for covariates (Antonsen *et al.,* 2020). In comparison, NO_2 and NO_x were significantly positively associated to schizophrenia hospitalisation (Antonsen *et al.,* 2020). Similarly, only $PM_{2.5}$ was non-significantly associated to schizophrenia outpatient visits however NO_2 was (Li *et al.,* 2020). Despite, more evidence $PM_{2.5}$ could have a negative impact on psychotic disorders in this review there was some variation in results. Variation could be due to differences in exposure periods, pollutant concentrations, participants, confounding, study designs, geographical location and even how the outcome was defined. Overall, the findings from this thesis further contribute to the literature showing the potential impact of air pollution on mental health.

In terms of the other mental health and well-being issues, $PM_{2.5}$ and NO_2 had a positive association with stress and distress. Whereas the associations were less consistent for the other mental health outcomes. Contradictory associations were found for anxiety, suicide and contact with mental health services. Although, a systematic review found a positive association between suicide mortality and short-term exposure to NO_2, SO_2, PM, CO (Davoudi *et al*., 2021) and PM (Liu *et al*., 2021). Although inverse associations were found for O_3 (Davoudi *et al*., 2021). Due to the lack of studies for the outcome's mania, self-harm and mortality linked to mental health it was difficult to come to any conclusions. However, both studies showed a positive significant association between self-harm and $PM_{2.5}$ (Liu *et al.,* 2018; Mok *et al.,* 2020). For the outcome self-reported mental health contradictory findings and heterogenous outcomes (various questionnaires) caused difficulties coming to conclusions. Moreover, the focus of most of the current literature is specific mental health conditions such as anxiety or depression not life satisfaction or general mental health. Dementia was excluded in the review due to the recent comprehensive COMEAP (2022) report on dementia and air pollution. In addition, depression was also excluded because of a recently published comprehensive systematic review and meta-analysis (Borroni *et al.,* 2021).

In the SAIL analysis, descriptive statistics were generated in terms of age, sex, deprivation, and urban/rural classification. The data supported the hypothesis since deprivation level affected the percentage of people with schizophrenia or OPD. In the analysis there was a higher percentage of schizophrenia or OPD diagnoses in most deprived areas (WIMD 1 and 2) particularly in the least deprived area (WIMD 1) compared to the least deprived areas (WIMD 5) (**Figure 3.3**). However, WIMD 3 and 4 had the same percentage of diagnoses which was only slightly more than in the least deprived areas (WIMD 5) (**Figure 3.3**). The other demographic variables, sex, age and rural or city residence did not show much variation between the schizophrenia or OPD cohort and the whole population. In addition, pollution levels which did not vary much between the two groups. The key finding from the descriptive statistics was the higher percentage of people with psychotic disorders in the most deprived areas compared to the least.

Other studies also found deprivation affected mental health. Numerous studies found a higher rate of schizophrenia and psychotic disorders in the more deprived neighbourhoods in the UK (Hardoon *et al.,* 2013; Omer *et al.,* 2014; Kirkbride *et al.,* 2015; O'Donoghue *et al.,* 2016a). Although there is limited research conducted on individuals in the prodromal stage (subclinical symptoms that precedes the onset of psychosis) which has resulted in conflicting findings (O'Donoghue *et al.,* 2016b). The potential cause of the association has not been definitively identified yet. However, there are two theories: social causation or social drift (Mossakowski *et al.,* 2014). The social causation hypothesis asserts that experiencing economic hardship increases the risk of subsequent mental illness (Mossakowski *et al.,* 2014). Whereas the drift hypothesis posits that mental illness can inhibit socioeconomic attainment cause people to live in hardship or to never escape poverty (Mossakowski *et al.,* 2014). The findings have implications for service provision such as location and access to services particularly in areas of deprivation (O'Donoghue *et al.,* 2016a). Therefore, knowing which areas to prioritise in terms of access and location to mental health treatment is vital due to limited resources (O'Donoghue *et al.,* 2016b).

4.1 Limitations and Future Research

The main limitations in the systematic review and SAIL data chapter were respectively:

- Heterogeneity of studies meant a meta-analysis was not performed and summarising the studies was challenging.
- It was not feasible to perform a regression in which confounders such as deprivation could have been included in the association between air pollution and psychotic disorders.

Limitations of the systematic review and SAIL analysis are explained in more detail in the discussions in each data chapter **2.4.1** and **3.41** respectively. Some of the knowledge gaps in relation to air pollution and mental health which need to be addressed by future research are summarised in **Table 4.1** below.

Table 4.1- The knowledge gaps in the relationship between air pollution and mental health including how these could be addressed.

Knowledge Gap	**How it could be addressed**
Identification of the most relevant time of exposure for the outcome of interest (acute vs. chronic exposure) (Hahad *et al.,* 2020). Since, individuals are exposed ubiquitously to air pollution and there can be short-term decreases in air quality.	More longitudinal cohort studies are necessary which follow up and observe individuals throughout their lives. Particularly as most of the research in this review investigated short-term exposures (58%) and often long-term was only investigating annual exposure.
Components of air pollution that might contribute to the development of mental disorders and which components could be more harmful or have synergistic effects (Braithwaite *et al.,* 2019).	Investigation of various pollutants and consider co-exposure to assist in understanding which pollutants could be the most hazardous to mental disorders (Braithwaite *et al.,* 2019).
Whether air pollution exposure contributes to the course and severity after the onset (Bakolis *et al.,* 2019).	Studies with participants which have already been diagnosed with a mental disorder and investigate disease progression, relapse, and severity.
Pollution has a negative effect physically which could have mental health impacts too (Ohrnberger *et al.,* 2017).	Include physical health as a confounder and investigate associations in vulnerable populations such as those with pre-existing conditions.
Identification of susceptible subpopulations to the effects of air pollution on mental health, *e.g.,* subjects with pre-existing conditions or with genetic susceptibility as well as the elderly and children (Hahad *et al.,* 2020).	More cohort studies which investigate childhood exposure to air pollution and future mental health service use. Additionally, exploration of the effects of air pollution in the general population compared to vulnerable groups such as those with chronic conditions or previous mental health support.

How confounding variables such as deprivation could affect any potential associations (CDC, 2004; Bakolis *et al.,* 2021).	Use of regressions which allow statistical associations between multiple variables to be investigated such as air pollution, mental health, and deprivation.
There is no universally accepted consistent definition for many mental health disorders and behaviours such as suicide ideation, which causes ongoing challenges for clinicians, researchers, and educators (Harmer *et al.,* 2022).	A globally recognised accurate definition for mental health and well-being terms as well as the development of objective biological tests (Kings *et al.,* 2018; Telles-Correia *et al.,* 2018).
In vitro and *in vivo* experiments linking air pollution to mental health to help identify the unknown causal mechanisms (Misiak, 2020, Bakolis *et al.,* 2021; Hahad *et al.,* 2020).	The DNA/RNA from human samples *e.g.*, nasal swabs could be used in PCR arrays to analyse the expression of genes involved in diagnosable mental health conditions after exposure to air pollution (Qiagen, 2020). A global approach could be used as, so far, no biomarkers have proven specificity and reproducibility to elucidate biomedical cues linking air pollution and mental health (Mora *et al*., 2018; García-Gutiérrez *et al*., 2020).

To appropriately answer these questions, it is important studies have a vigorous methodology and large enough sample sizes to demonstrate meaningful effects.

Research into air pollution and mental health is vital as the consequences of not addressing rising pollution levels and mental disorders is dire (Patel *et al.,* 2018). The need for this research is emphasised by the unmet needs for mental health care in terms of routinely worse quality services compared to physical health and government investment remains small (Patel *et al.,* 2018). Moreover, air pollution and climate change are the biggest environmental threats to human health. These threats come from reduced health, mortality and natural disasters which impact mental health negatively as explained in the introduction (Thomson *et al.,* 2018; Romanello *et al.,* 2022). If globally governments subsidised alternatives and regulated air pollution levels further this could contribute to potentially alleviating the pressure on mental health services and tackling climate change (Shaddick *et al.,* 2020). Pressure on mental health services could also be reduced by improving access and providing more support in deprived areas. However, collective failure to respond to the increasing need to reduce air pollution and improve mental health services could result in huge financial loss and avoidable suffering (Patel *et al.,* 2018).

5 Conclusion

Having examined the evidence in the systematic review, PM and NO_2 were the most hazardous pollutants to well-being *e.g.,* stress, and severe mental disorders *e.g.,* schizophrenia. The data linkage study also found $PM_{2.5}$ had a positive correlation with psychotic disorders. However, it is important to recognise that more research is still required because of contradictory findings and knowledge gaps identified. For example, the unknown causal mechanism and understanding of the influence of deprivation on any potential associations. However, overall, the evidence suggests that reducing air pollution could have holistic benefits in terms of both physical and mental health.

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7 Appendices

Appendix A: Code Used in SAIL

A.1 Installation

```
install.packages("sailr");
library(sailr);
install.packages("tidyverse")
library(tidyverse)

conn <- sail_open();

q <- "SELECT * FROM SAILW1413V.JL_COHORT";
```

A.2 Descriptive Statistics for All Participants

```
#Number of all participants
nrow(data)

#Male (1)
sum(data$gndr_cd==1)
#Female (2)
sum(data$gndr_cd==2)

#Min, Q1, Median, Mean, Q3, Max Age
summary(data$age)

#Environment
unique(data$urban_rural_inception)
#Rural and fringe
sum(data$urban_rural_inception=="Rural town and fringe")
sum(data$urban_rural_inception== "Rural village and dispersed in a
sparse setting")
```

```
sum(data$urban_rural_inception=="Rural town and fringe in a sparse
setting")
sum(data$urban_rural_inception=="Rural village and dispersed")
#City and town
sum(data$urban_rural_inception=="Urban city and town")
sum(data$urban_rural_inception=="Urban city and town in a sparse
setting")

#Deprivation
unique(data$wimd2019_quintile_desc_inception)
sum(data$wimd2019_quintile_desc_inception=="1. Most deprived ")
sum(data$wimd2019_quintile_desc_inception=="2                ")
sum(data$wimd2019_quintile_desc_inception=="3                ")
sum(data$wimd2019_quintile_desc_inception=="1. Least deprived ")
```

A.3 Descriptive Statistics of the Schizophrenia and OPD Cohort

```
#All
sum((data$opd==1||data$schiz==1),na.rm=T)

# People with only schiz
sum((data$schiz==1&data$opd!=1),na.rm=T)
# People with only OPD
sum((data$opd==1&data$schiz!=1),na.rm=T)
# People with both
sum((data$opd==1&data$schiz==1),na.rm=T)

#Sex
sum(((data$opd==1|data$schiz==1)&(data$gndr_cd==2)),na.rm=T)

#Min, Q1, Median, Mean, Q3, Max Age
summary(data$age, data$opd==1|data$schiz==1)

#Rural and fringe
sum((data$urban_rural_inception=="Rural town and fringe")
&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$urban_rural_inception== "Rural village and dispersed in a
sparse setting")&(data$opd==1|data$schiz==1),na.rm=T)
```

```
sum((data$urban_rural_inception=="Rural town and fringe in a sparse setting")&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$urban_rural_inception=="Rural village and dispersed")&(data$opd==1|data$schiz==1),na.rm=T)

#City and town
Sum((data$urban_rural_inception=="Urban city and town")&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$urban_rural_inception=="Urban city and town in a sparse setting")&(data$opd==1|data$schiz==1),na.rm=T)

#Deprivation
sum((data$wimd2019_quintile_desc_inception=="1. Most deprived ")&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$wimd2019_quintile_desc_inception=="2 ")&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$wimd2019_quintile_desc_inception=="3 ")&(data$opd==1|data$schiz==1),na.rm=T)
sum((data$wimd2019_quintile_desc_inception=="1. Least deprived ")&(data$opd==1|data$schiz==1),na.rm=T)
```

A.4 Air Pollution Values

```
#Air pollutants for All Participants
summary(data$pm10_mean)
summary(data$pm25_mean)
summary(data$nox_mean)

#Air pollutants Schizophrenia and Other Psychotic disorders Cohort
summary(subset(data, data$opd==1|data$schiz==1))
```

A.5 Code used to create Boxplots and Histograms

```
#Type of distribution
#PM10
boxplot(data$pm10_mean)
hist(data$pm10_mean)

#PM2.5
boxplot(data$pm25_mean)
hist(data$pm25_mean)

#NOx
boxplot(data$nox_mean)
hist(data$nox_mean)
```

A.6 Correlation code

```
library(sailr);
conn <- sail_open();
q <- "SELECT * FROM SAILW1413V.JL_COHORT";
data <- sail_query(conn, q);
```

A.6.1 NO_x and the Percentage of people with Schizophrenia or OPD

```
#NOx and schiz_OPD frequency table
mh_freq_NOx_t<-
table(as.integer(data$nox_mean),data$opd==1|data$schiz==1)
print(mh_freq_NOx_t)

#converting the table into a dataframe
mh_freq_NOx_df<-as.data.frame(mh_freq_NOx_t)
print(mh_freq_NOx_df)

#change_col_names
colnames(mh_freq_NOx_df)<-c('NOx_conc','na','mh_freq')
print(mh_freq_NOx_df)

#Exclude people without the condition
mh_freq_NOx_df<-subset(mh_freq_NOx_df,na==TRUE)
print(mh_freq_NOx_df)

#population_table
#concentrations above 0
pop_freq_NOx_t<-table(as.integer(data$nox_mean),data$nox_mean>0)
print(pop_freq_NOx_t)

#converting the table into a dataframe
pop_freq_NOx_df<-as.data.frame(pop_freq_NOx_t)
print(pop_freq_NOx_df)

#change_col_names
colnames(pop_freq_NOx_df)<-c('NOx_conc','na','pop_freq')
print(pop_freq_NOx_df)
```

```
#merge the schiz/opd dataframe and population frequency dataframe
mh_percent_NOx_df=merge(x=mh_freq_NOx_df, y=pop_freq_NOx_df,
by='NOx_conc')
mh_percent_NOx_df

#Calculate the percentage of people with schiz/OPD in the population
mh_percent_NOx_df$percent_mh_NOx <-
(mh_percent_NOx_df$mh_freq/mh_percent_NOx_df$pop_freq)*100
mh_percent_NOx_df

#Correlation_test
cor.test(x=as.numeric(mh_percent_NOx_df$NOx_conc),
y=as.numeric(mh_percent_NOx_df$percent), method='spearman')

#Scatter_graph
plot(x=as.numeric(mh_percent_NOx_df$NOx_conc),
y=as.numeric(mh_percent_NOx_df$percent))
```

A.6.2 $PM_{2.5}$ and the Percentage of people with Schizophrenia or OPD

```
#PM2.5
mh_freq_PM2.5_t<-
table(as.integer(data$pm25_mean),data$opd==1|data$schiz==1)
print(mh_freq_PM2.5_t)

mh_freq_PM2.5_df<-as.data.frame(mh_freq_PM2.5_t)
print(mh_freq_PM2.5_df)

#change_col_names
colnames(mh_freq_PM2.5_df)<-c('PM2.5_conc','na','mh_freq')
print(mh_freq_PM2.5_df)

mh_freq_PM2.5_df<-subset(mh_freq_PM2.5_df,na==TRUE)
print(mh_freq_PM2.5_df)

#concentrations above 0
pop_freq_PM2.5_t<-table(as.integer(data$pm25_mean),data$pm25_mean>0)
print(pop_freq_PM2.5_t)

pop_freq_PM2.5_df<-as.data.frame(pop_freq_PM2.5_t)
print(pop_freq_PM2.5_df)

colnames(pop_freq_PM2.5_df)<-c('PM2.5_conc','na','pop_freq')
print(pop_freq_PM2.5_df)

mh_percent_PM2.5_df=merge(x=mh_freq_PM2.5_df, y=pop_freq_PM2.5_df,
by='PM2.5_conc')
mh_percent_PM2.5_df

mh_percent_PM2.5_df$percent_mh_PM2.5 <-
(mh_percent_PM2.5_df$mh_freq/mh_percent_PM2.5_df$pop_freq)*100
mh_percent_PM2.5_df
```

```
#Correlation
cor.test(x=as.numeric(mh_percent_PM2.5_df$PM2.5_conc),
y=as.numeric(mh_percent_PM2.5_df$percent), method='spearman')

plot(x=as.numeric(mh_percent_PM2.5_df$PM2.5_conc),
y=as.numeric(mh_percent_PM2.5_df$percent))
```

A.6.3 PM_{10} and the Percentage of people with Schizophrenia or OPD

```
#PM10
mh_freq_PM10_t<-
table(as.integer(data$pm10_mean),data$opd==1|data$schiz==1)
print(mh_freq_PM10_t)

mh_freq_PM10_df<-as.data.frame(mh_freq_PM10_t)
print(mh_freq_PM10_df)

#change_col_names
colnames(mh_freq_PM10_df)<-c('PM10_conc','na','mh_freq')
print(mh_freq_PM10_df)

mh_freq_PM10_df<-subset(mh_freq_PM10_df,na==TRUE)
print(mh_freq_PM10_df)

#concentrations above 0
pop_freq_PM10_t<-table(as.integer(data$pm10_mean),data$pm10_mean>0)
print(pop_freq_PM10_t)

pop_freq_PM10_df<-as.data.frame(pop_freq_PM10_t)
print(pop_freq_PM10_df)

colnames(pop_freq_PM10_df)<-c('PM10_conc','na','pop_freq')
print(pop_freq_PM10_df)

mh_percent_PM10_df=merge(x=mh_freq_PM10_df, y=pop_freq_PM10_df,
by='PM10_conc')
mh_percent_PM10_df

mh_percent_PM10_df$percent_mh_PM10 <-
(mh_percent_PM10_df$mh_freq/mh_percent_PM10_df$pop_freq)*100
mh_percent_PM10_df

#Correlation
```

```
cor.test(x=as.numeric(mh_percent_PM10_df$PM10_conc),
y=as.numeric(mh_percent_PM10_df$percent), method='spearman')

plot(x=as.numeric(mh_percent_PM10_df$PM10_conc),
y=as.numeric(mh_percent_PM10_df$percent))
```

Appendix B: Data for the Correlation Graphs

Table B.1- Contains the number of people with OPD or schizophrenia and the total population exposed to a specific concentration of NO_x used to calculate the percentage of people with OPD or schizophrenia per pollutant concentration. The pollutants from 37 to 54 contained numbers of people less than 5 so multiple concentrations were combined (37-39, 40-45 and 46-54).

NO_X concentration (μg/m^3)	**Number of people with OPD or schizophrenia**	**Total population number**	**Percentage of people with OPD or schizophrenia (%)**
3	0	957	0
4	59	87278	0.0676
5	123	136576	0.09006
6	61	75671	0.080612
7	78	79059	0.09866
8	69	81436	0.084729
9	64	88140	0.072612
10	131	119372	0.109741
11	97	125381	0.077364
12	86	96697	0.088938
13	92	95973	0.09586
14	100	105386	0.094889
15	95	102358	0.092812
16	75	79728	0.09407
17	94	85576	0.109844
18	49	66374	0.073824
19	59	60512	0.097501
20	62	60106	0.103151
21	35	36775	0.095173
22	39	43935	0.088767
23	41	43613	0.094009
24	29	32344	0.089661
25	24	28310	0.084776
26	11	14240	0.077247
27	19	32327	0.058774

28	31	37990	0.0816
29	32	38011	0.084186
30	25	25190	0.099246
31	14	20281	0.06903
32	22	28165	0.078111
33	18	22487	0.080046
34	9	14004	0.064267
35	7	9834	0.071182
36	7	10950	0.063927
37-39	8	20214	0.039577
40-45	12	9939	0.120736
46-54	7	10454	0.06696

Table B.2- Contains the number of people with OPD or schizophrenia and the total population exposed to a specific concentration of $PM_{2.5}$ which was used to calculate the percentage of people with OPD or schizophrenia per pollutant concentration. The pollutant with a concentration of 16 contained a number of people less than 5 so the concentrations 15 and 16 were combined.

$PM_{2.5}$ concentration (μg/m^3)	Number of people with OPD or schizophrenia	Total population number	Percentage of people with OPD or schizophrenia (%)
4	7	8956	0.078159893
5	198	246591	0.080294901
6	394	441653	0.089210308
7	705	765171	0.092136268
8	340	384544	0.08841641
9	116	146926	0.078951309
10	24	27969	0.085809289

Table B.3- Contains the number of people with OPD or schizophrenia and the total population exposed to a specific concentration of PM_{10} which was used to calculate the percentage of people with OPD or schizophrenia per pollutant concentration.

PM_{10} concentration (µg/m^3)	**Number of people with OPD or schizophrenia**	**Total population number**	**Percentage of people with OPD or schizophrenia (%)**
7	19	22930	0.082860881
8	135	162009	0.083328704
9	100	135199	0.073965044
10	293	313220	0.093544474
11	527	583975	0.090243589
12	424	440654	0.096220618
13	186	215601	0.086270472
14	75	114588	0.06545188
15-16	25	33634	0.074329547